PROSPECTIVE STUDY OF DIFFUSION TENSOR IMAGING AND CONVENTIONAL MAGNETIC RESONANCE IMAGING IN TERM AND PRETERM NEONATES WITH HYPOXIC ISCHEMIC ENCEPHALOPHY AND CORRELATION WITH CLINICAL OUTCOME

Dissertation submitted to

THE TAMILNADU Dr.M.G.R. MEDICAL UNIVERSITY

In partial fulfillment of the requirements

Of

M.D. DEGREE EXAMINATION

BRANCH- VIII- RADIODIAGNOSIS

GOVT KILPAUK MEDICAL COLLEGE

CHENNAI- 600010

THE TAMILNADU DR.M.G.R. MEDICAL UNIVERSITY

CHENNAI- TAMILNADU, INDIA

MAY 2019

CERTIFICATE

This is to certify that the dissertation **"PROSPECTIVE STUDY OF DIFFUSION TENSOR IMAGING AND CONVENTIONAL MAGNETIC RESONANCE IMAGING IN TERM AND PRETERM NEONATES WITH HYPOXIC ISCHEMIC ENCEPHALOPHY AND CORRELATION WITH CLINICAL OUTCOME"** titled submitted by **Dr.S.USHA** appearing for **M.D(RADIODIAGNOSIS)** degree examination in May 2019 is a bonafide record of work done by her under my guidance and supervision in partial fulfillment of requirement of the Tamilnadu Dr.M.G.R. Medical University, Chennai. I forward this to the TamilNadu Dr.M.G.R Medical University, Chennai.

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DECLARATION

I Dr. S.USHA, solemnly declare that this dissertation **PROSPECTIVE STUDY OF DIFFUSION TENSOR IMAGING AND CONVENTIONAL MAGNETIC RESONANCE IMAGING IN TERM AND PRETERM NEONATES WITH HYPOXIC ISCHEMIC ENCEPHALOPHY AND CORRELATION WITH CLINICAL OUTCOME** is a bonafide work done by me at Government Kilpauk Medical College, under the supervision of **Dr.J.DEVIMEENAL DMRD, DNB, MD, FRCR,** Professor, Government Kilpauk Medical College. This dissertation is submitted to the Tamil Nadu Dr. M.G.R Medical University, towards partial fulfillment of requirement for the award of M.D. Degree Radiodiagnosis.

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CERTIFICATE – II

This is to certify that this dissertation work titled entitled dissertation **PROSPECTIVE STUDY OF DIFFUSION TENSOR IMAGING AND CONVENTIONAL MAGNETIC RESONANCE IMAGING IN TERM AND PRETERM NEONATES WITH HYPOXIC ISCHEMIC ENCEPHALOPHY AND CORRELATION WITH CLINICAL OUTCOME** of the candidate **Dr. S.USHA** with Registration Number **201518253** for the award of **M.D** degree in the branch of **RADIODIAGNOSIS**. I personally verified the urkund.com website for the purpose of plagiarism check. I found that the uploaded thesis file contains from introduction to conclusion pages and result shows **7%** of plagiarism in this dissertation.

Guide & Supervisor sign with Seal.

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CONTENTS

INTRODUCTION

Case Definition:

Hypoxic ischemic encephalopathy

HIE is a brain dysfunction caused by a reduction in the supply of oxygen to the brain and other organs (hypoxia), compounded by low blood flow to vital organs (ischemia). Encephalopathy refers to any condition that results from reduced blood and oxygen supply to the brain. **Perinatal asphyxia**, or **birth asphyxia** is deprivation of oxygen to a newborn infant that lasts long enough during the birth process to cause injury to the brain[1].

Hypoxic injury occurs before 35 weeks of gestational age results in periventricular leucomalacia. At 40 weeks of gestational age ,the degree of hypoxia correlates to the area of the brain that is injured. Mild hypoxia will affect the parasagittal white matter while severe hypoxia affects the putamen, thalamus and paracentral white matter.

Certain signs may appear shortly after birth like organ dysfunction (heart, kidney, lung and liver) denotes possible HIE. Seizure in the first 24 hours of life can also denotes in the possibility of HIE.

Imaging methods attributed to better understanding of pathological events also allows quantitative monitoring of disease progression that may provide decision regarding intervention like stimulation therapy and physiotherapy.

Conventional MRI sequences can help to exclude other causes of encephalopathy such as hemorrhage, cerebral infarction , neoplasm or congenital malformation. Eight months appear to be the earliest time at which MRI findings are correlate well with the developmental outcome. In predicting neurological outcome MRI findings of the neonatal period had the highest negative predictive value[2].

DTI provides qualitative and quantitative information about the Micro structure of white matter that can not be deducted by the conventional MRI sequences. DTI provides transcending MRI from anatomic images toward functional and embryology based imaging.

DTI enables quantitative analysis and structural analysis that may be created through post processing and reconstructing the course of fibre tracts. Due to incomplete myelination and higher brain water content in term neonates conventional MRI has limited in its ability to detect the presence and extend of injury in stage 1 HIE. Structural changes usually manifested after 4 to 8 months infants with HIE stage 1 and 2.

DTI imaging demonstrates abnormal Fractional anisotrophy and mean diffusivity values in HIE infants even when they shows near normal conventional imaging. An altered pattern of age related changes in Fractional anisotrophy and mean diffusivity and accurate assessment of micro structural damage also been demonstrated with DTI. [3]

HIE is the common cause of cerebral palsy. Cerebral palsy is defined as a group of permanent disorders of the development of movement and posture, causing activity limitation, that are due to non-progressive disturbances that occurred in the developing fetal or infant brain. Early assessment of severity of HIE can help proper parent counseling and early institution of stimulation therapy for better development of infant. So there is a necessity to study the importance of DTI in detecting HIE babies within 14 days of their life.

REVIEW OF LITERATURE

Hypoxic ischemic encephalopathy (HIE) is one of the dreadful birth complication. In developed countries it occurs in 1.5 to 2.5 per 1000 live births . **Lawn J et al**., **2005** discovered that the incidence is up to 10-fold higher in developing countries and globally, 23% of the 4 million annual neonatal deaths are due to birth asphyxia.

During the prenatal, intrapartum or postnatal period, HIE can occur due to inadequate blood flow to the infant's brain occurring as a result of a hypoxic-ischemic event.

As says by **Liska A, et al**.and **Azzopardi D, et al.** by the age of 2 years, 60% of infants with HIE will experience severe disabilities including cerebral palsy, mental retardation and seizures. Even with advances in obstetric care and fetal monitoring the incidence of HIE has not declined. [3,4,5,6]

HIE is spectrum with clinical manifestations of brain dysfunction . Exact cause is not appreciable always [7] some causative factors are placenta previa, abruptio placenta, maternal hypotension, uterine rupture, cord prolapse, breech presentation and shoulder dystocia.

In perinatal HIE in early postnatal life manifestations include poor umbilical cord gases (pH < 7.0 or base deficit ≥ 12 mmol/L)[8] ,presence of meconium stained fluid, abnormal fetal heart rate tracings[9] ,low Apgar scores [10] ,respiratory support within the first several minutes of postnatal life. [11]

Another Sarnat staging criteria or an adapted version is also followed to describe the severity of encephalopathy within the first several postnatal days of life to assess the severity of the insult.

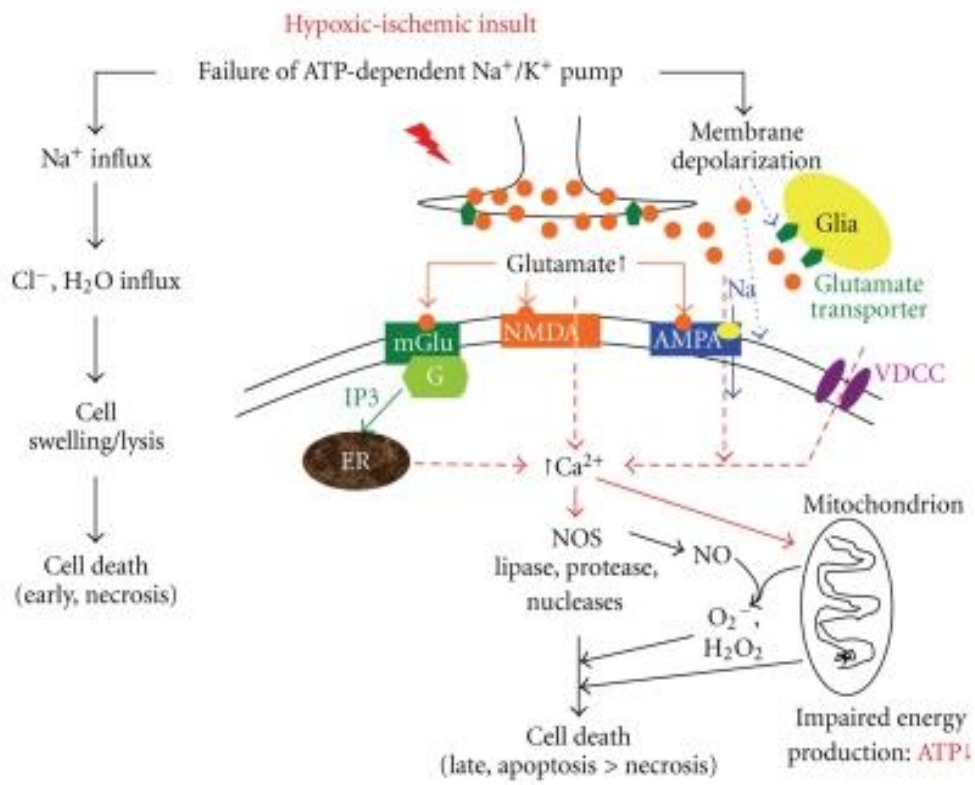
Following Table(1) shows neonatal encephalopathy staging criteria.[12]

TABLE - 1

Sarnet Stages of Neonatal Encephalopathy

Assessment	Stage 1	Stage 2	Stage 3
Mental status	Hyperalert	Lethargic	Stuporous
Suck reflex	Weak or absent	Weak or absent	Absent
Moro reflex	Strong	Weak	Absent
Muscle tone	Normal	Hypotonia	Flaccid
Autonomic function	Generalized sympathetic	Generalized parasympathetic	Absent
Pupils	Mydriasis	Miosis	Variable
Seizures	None	Common	Variable
EEG	Normal (awake)	Early: low-voltage theta and delta	Early: periodic pattern with isopotential phases Late: isopotential
Duration	< 24 hours	2–14 days	Hours to weeks

FIGURE - 1



When there is a decrease in high-energy phosphates it causes acute influx of Na+, Cl− and water that can cause cell death (necrosis) in severe insult, but in less severe insult, it causes membrane depolarization resulting in a series of excitotoxicity and oxidative stress leading to delayed cell death, that is apoptosis.[13]

Continuous membrane depolarization results in a increased amount of presynaptic glutamate release, reversal of glutamate transport in glia and nerve endplates and activation of NMDA and immature AMPA receptors with increased Ca2+ influx with a series of Ca2+-mediated apoptosis.

As says by **Zipursky A. et al** harmful effects of cytosolic Ca2+ are destruction of cellular lipids by activation of phospholipase and of cellular DNA by activation of nucleases and production of free radicals and nitric oxide (NO) by increase of nitric oxide synthase (NOS) [14,15,16]. (AMPA: α-amino-3-hydroxyl-5-methyl-4-isoxazole-propionate; ER: endoplasmic reticulum; mGlu: metabotropic glutamate; NMDA: N-methyl-D-aspartic acid; NOS: nitric oxide synthase; VDCC: voltage-dependent calcium channels)

CEREBRAL PALSY

A group of permanent disorders in the development of posture and movement due to non-progressive disturbances in the developing brain is called as cerebral palsy. Motor disorders in cerebral palsy characterised by disturbances of mental ability, sensation, perception, behaviour and communication epilepsy and secondary musculoskeletal problems can also co-occur with CP.

Motor function impairment will lead to involuntary movement, in coordination or paresis. Motor disorders which are transient, that result from progressive disease of the brain, or that are due to spinal cord abnormalities/injuries are not included in CP.

HYPOXIC ISCHEMIC INJURY IN DEVELOPING BRAIN

Bonfoco E, et al.says that Hypoxic–ischaemic injury patterns of brain injury vary according to the nature and severity of the insult and the degree of maturity of the developing brain [17] [18]

Partial hypoxic–ischaemic injury denotes single episode or episodes of hypoxia or hypoperfusion to the developing brain, profound hypoxic–ischaemic injury is described as short episode of anoxia or circulatory arrest. Injuries occurring in the first and early part of the second trimester of pregnancy causes brain malformations.

PRETERM PATTERNS

The ‘preterm’ patterns of hypoxic–ischaemic injury seen in brains of about 20–35 weeks gestational age and neonatal encephalopathy is seen .

Some babies survive a profound hypoxic–ischaemic injury, but if they survive, there is predominant injury in the thalami with relative sparing of the other deep grey matter structures.

Partial hypoxic–ischaemic injury causes periventricular leukomalacia (PVL), germinal matrix or periventricular haemorrhage and intraventricular haemorrhage (GM/IVH), also called as periventricular haemorrhagic infarction (PVHI) [19] [20]. In severe cases, cystic encephalomalacia can be seen.

Mechanism for this condition is considered to be a complication of prematurity and is probably multifactorial.

The presentation is spastic diplegia or quadriplegia, often with visual impairment. Mental retardation is usually absent, except in very extreme cases, as are seizures[21].

Another theory states that there is cerebral hypoperfusion and hypoxia causing ischaemic infarction, in which 18% may be complicated by secondary haemorrhage following reperfusion of the damaged areas. The areas of the immature brain most sensitive to decreased cerebral perfusion or hypoxia are seen in the periventricular white matter, which is the most common location.

Hagberg G, et al says that risk factors such as sepsis, necrotizing enterocolitis, respiratory problems, feto-maternal haemorrhage, or hypoglycaemia are associated with PVL. Infarction with oedema seen in the periventricular region is seen in PVL. This may be seen on Ultrasound as increased echogenicity[22].

Cystic degeneration occurs in damaged tissue 10–20 days after the insult. Small confluent cysts form in the periventricular white matter; these are usually transient and they subsequently collapse.

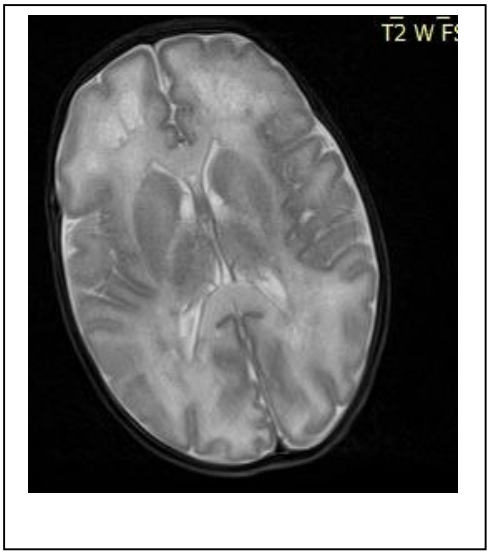
These cysts is the most reliable US finding of PVL in its early development .Collapse of cysts is followed by atrophy of the damaged brain tissue and this process is first detected by secondary ventricular dilatation; in more severe cases there will be more loss of brain tissue, commonly the white matter[22].

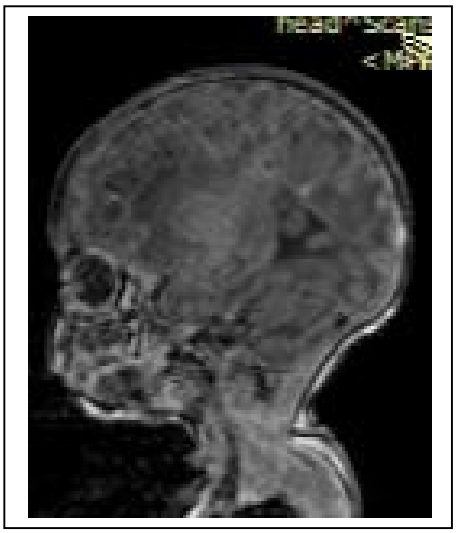
4–8 weeks after injury, the ventricular dilatation is detectable by US or CT, depending on severity of the lesions, and persists throughout life as permanent tissue loss. Decreased amount of periventricular white matter adjacent to the trigones result in end-stage PVL.

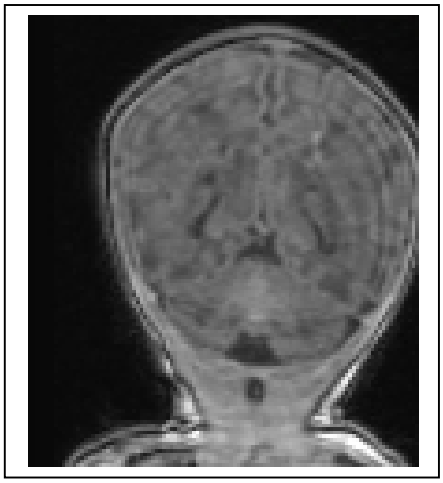
There is ventricular dilatation with irregular ventricular margins and the distribution is worst in the parieto-occipital regions [22]

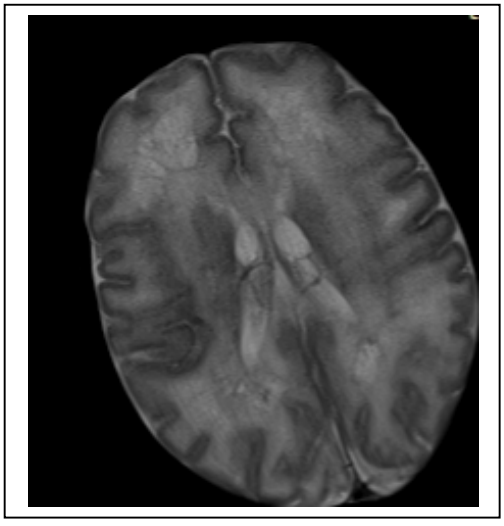
MRI is most reliable in demonstrating end-stage changes of PVL, 1–2 years after the injury, when the myelination process is almost complete. MRI also shows abnormal signal in the remaining periventricular white matter.

FIGURE - 2









- T2W hyperintensitywith restricted diffusionin bilateral cerebral periventricular and deep white matter,corpus callosum, internal capsule,cerebral peduncle and anterior pons.
- Myelination of posteror internal capsule is absent.
- Few tiny T1W hyperintensities in perilateral ventricular white matter.

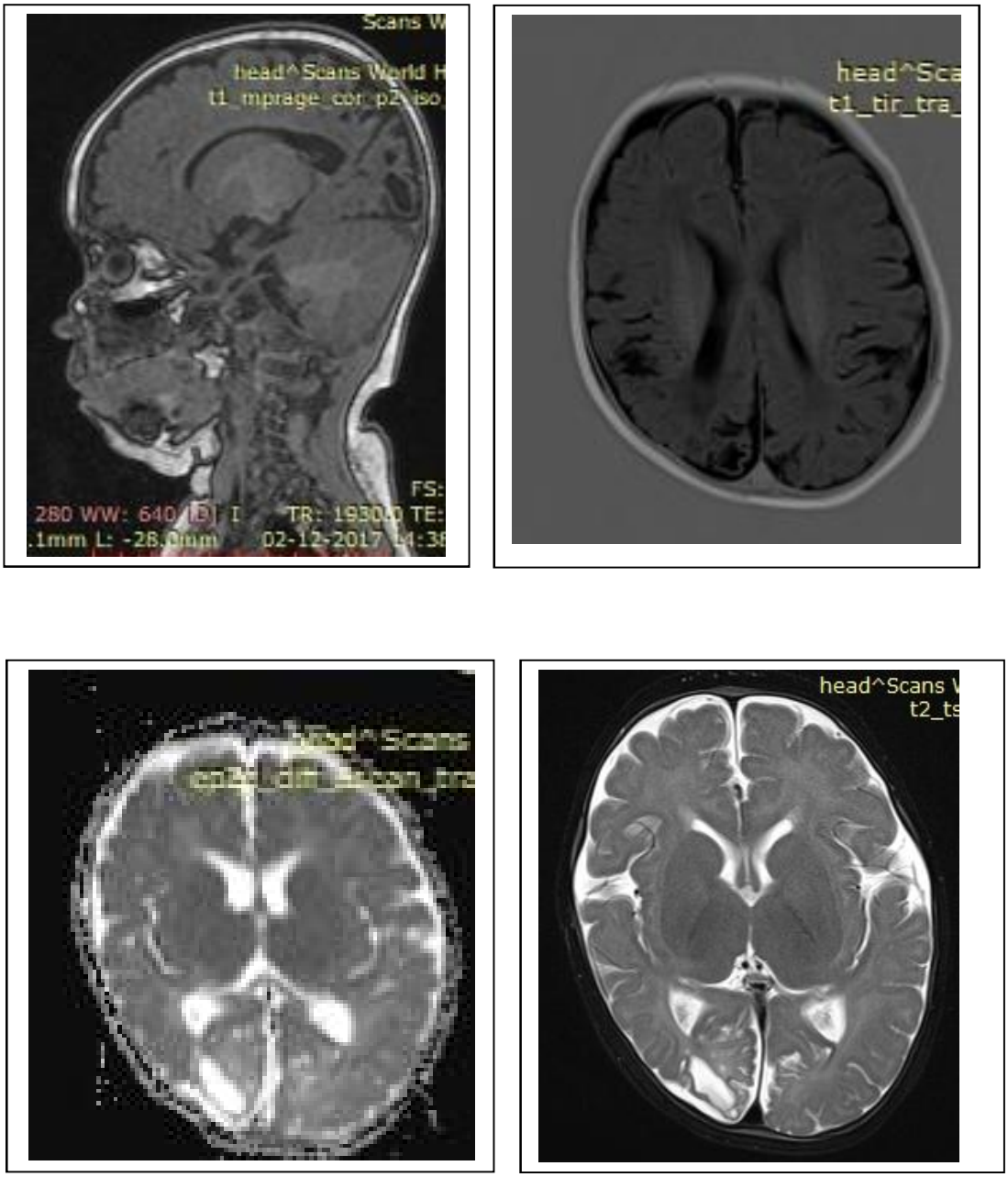
TERM PATTERNS

The ‘term’ patterns of hypoxic–ischaemic injury is seen in brains of 36–42 weeks gestational age at the time of the insult. The pattern characteristic of profound hypoxic–ischaemic injury mainly affects the brain regions which are most metabolically active that are the ventrolateral thalami, posterolateral putamina and adjacent capsular white matter, the hippocampi, peri-Rolandic (motor and sensory) cortex and visual cortex.

The changes are symmetrical and bilateral. The cerebellar vermis is selectively vulnerable. This pattern is in parallel with the clinical picture of dyskinetic or dystonic cerebral palsy [(22)]

The injuries mentioned in cases of partial hypoxic ischaemia are seen in a parasagittal areas, usually involving a combination of cortex and subcortical white matter, and also across the frontoparietal regions. usually bilateral, this pattern can also be asymmetric. A common region of involvement is the posterior part of the Sylvian fissures. The most severe injury is seen at the base of the gyri, within the depths of the sulci, causing focal atrophy in these areas and a pattern recognized as ulegyria

FIGURE - 3



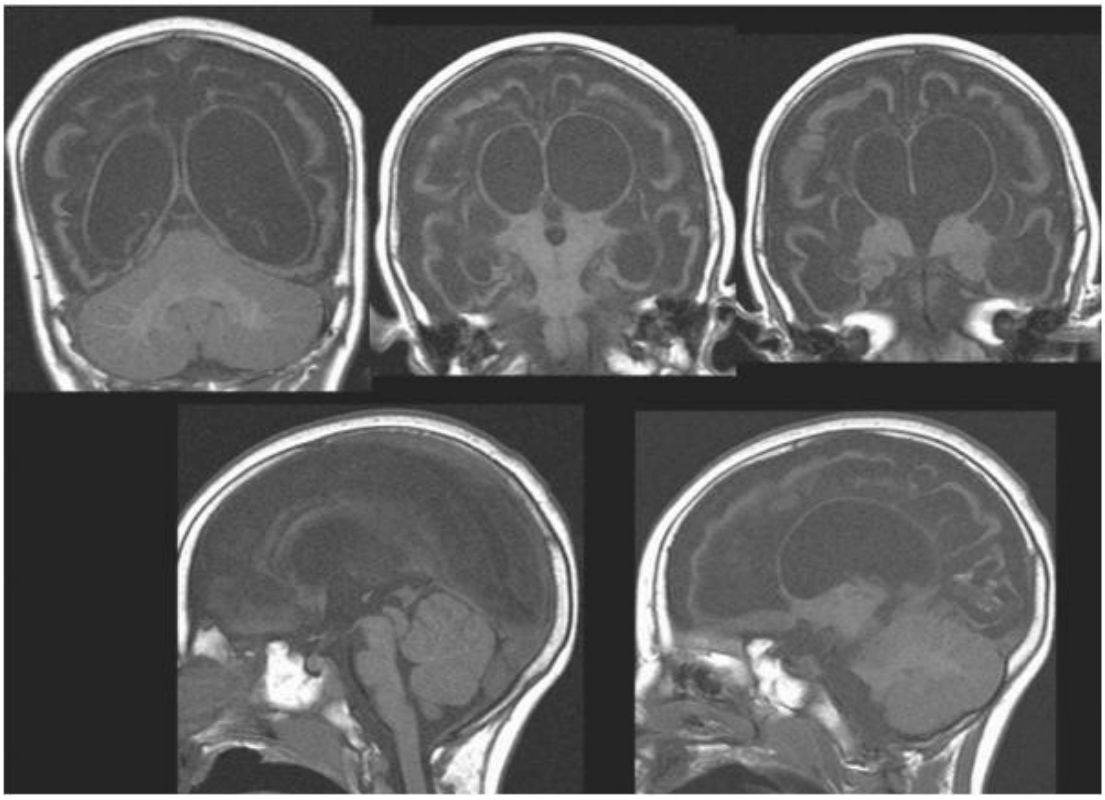
Gliosis in bilateral parietooccipital region.

Thinning of posterior body and splenium of corpus callosum.

Mild exvacuo prominence of occipital horns of both lateral ventricle.

In preterm, more prolonged insults causes cystic encephalomalacia (Fig.4). The characteristic involvement of the cerebral hemipheres with relative sparing of the posterior fossa structures which favours HIE .

FIGURE - 4



Multicystic encephalomalacia due to Prolonged hypoxic ischaemia. Note the cystic cavitation of most of the white matter with grossly thinned corpus callosum, leaving only a thin rim of preserved cortical mantle.[22]

DTI and fiber tractography (FT) are the recent methods that shows the orientation and integrity of white matter fibers in vivo [23] Previous studies evaluated axonal damage due to chronic infarct or motor neuron disease [24], a direct damage to axonal fibers such as multiple sclerosis [25,26], or acute disseminated encephalomyelitis.

Both congenital and postnatal developmental central nervous system (CNS) diseases, employs DTI due to its potential for generating a fiber pathway and aberrant connections in the case of a blockage of normal white matter formation. Developmental CNS anomalies with DTI and FT and their clinical usefulness is explaining the aberrant fiber connections to provide a better understanding is establised.[27]

Neonatal encephalopathy associated with perinatal hypoxia-ischemia is a leading cause of neonatal mortality and permanent neurological disability.

Perinatal asphyxia accounts for 10–20% of cases of cerebral palsy and 30% risk of disabilities including autism, global developmental delay, epilepsy, blindness, deafness and problems with cognition, memory, fine motor skills, and behavior. **[22]**

NORMAL MYELINATION MILESTONES

In infant brain the extent of myelination can be assessed by MRI according to specific milestones. During brain maturation there is progressive T2 and T1 shortening of the white matter because of changes in the lipid and water content of developing myelin and packing of white matter tracts[28].

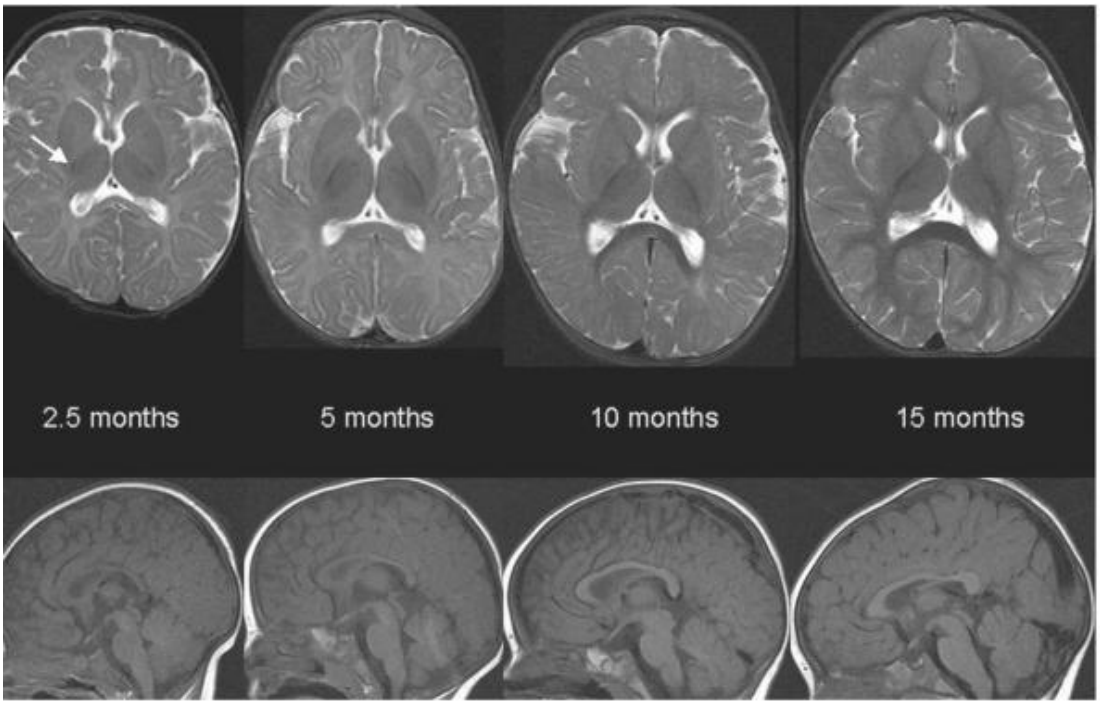
It occurs in the order of posterior-to-anterior , inferior-to-superior and centrifugal pattern and is complete by the age of 2 years(FIG 5)

Barkovich AJ, et al and Peded S, et al says that modern advanced MRI shows increased fractional anisotropy (assessed by diffusion tensor imaging), progressive reduction in water diffusion and increased magnetization transfer [29,30,31]

White matter tracts myelination is detected in the earlier on T1-weighted spin-echo (SE) or inversion recovery (STIR) sequences and in grey matter earlier on T2-weighted fast spin-echo (FSE).

Myelination occurs post-term in the first 8 months, sometimes extend into adulthood. Brain appears completly myelinated on T2-weighted sequences by 2 years, with almost an adult appearance on T1-weighted sequences by 10 months.

FIGURE - 5



Normal brain development with age seen on T2- (first row) and T1-weighted (second row) MRI.

Myelination at term and at 2.5 months in T2-weighted sequences are seen centrally as signal hypointensity within the posterior limbs of the internal capsules. This proceedes from posterior to anterior with age. On T2-weighted images myelination also progresses from central to peripheral.

In sagittal T1-W sequences there is progressive bulking up of the corpus callosum. By 6 months the corpus callosum becomes its normal childhood size. Genu is slightly smaller than splenium.

The newborn has a well-developed sensory system but limited motor function. So myelination pattern noted in full term is primarily in the sensory tracts. In the first 6 months of life the process of myelination is very easy to follow on T1-w images, where the myelinated areas appear bright.

T2-w images takes much more myelin to produce a hypointense signal within the white matter hence they are less sensitive .

In full term babies, T1-w images show high signal in the dorsal medulla and brain stem, the central corona radiata, about a third of the posterior limb of the internal capsule, the cerebellar peduncles, a small part of the cerebral peduncles and the deep white matter in the region of the pre- and post-central gyrus[32].

Myelination progression is seen in the optic radiations during the first months of life. By 3 months internal capsule will demonstrate T1 shortening within the anterior limb, but on T2-w images the hypointensity due to myelin is seen after 8 months.

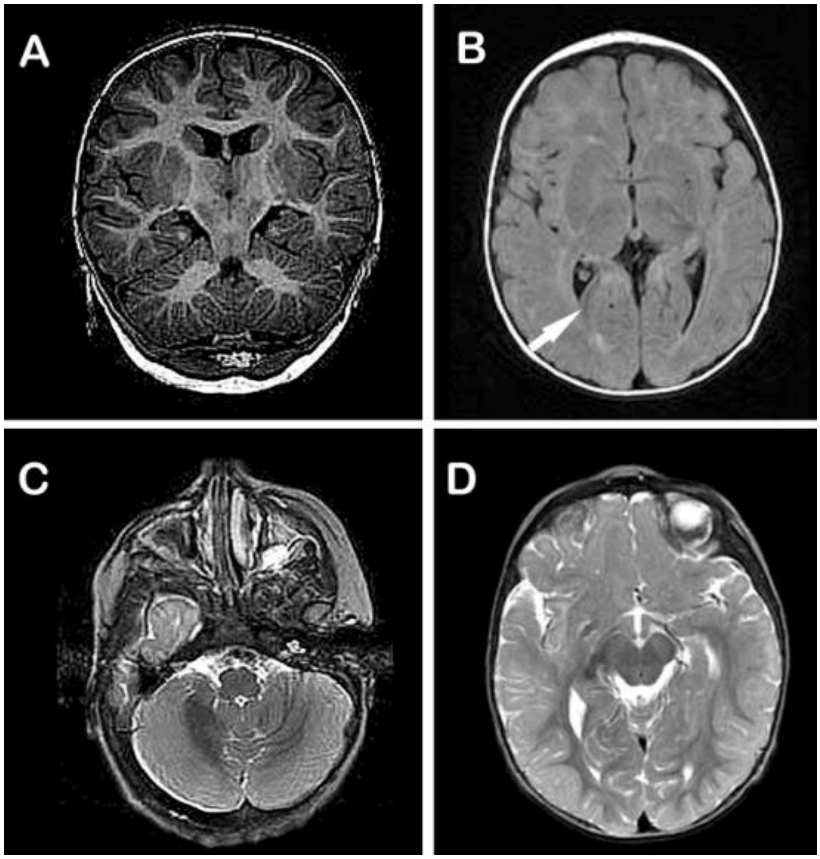
Preiss S, et al says that at 3 months of age the splenium of the corpus callosum on T2-w images becomes hypointense which extends anteriorly along the body and genu, and the complete corpus callosum is myelinated at 6 months[33].

By 10 months of age the brain is fully myelinated by T1 criteria.T2-weighted images are then used to assess the myelination from 6 months to 24 months of age, though the milestones of myelination are not so precise than during the first 6 months of life.

First signs of mature subcortical white matter are found around the calcarine fissure on T2 w images at 4 months and in the pre- and post-central gyri at 8 months. By 10 months the occipital subcortical white matter appears isointense. This process proceeds anteriorly and by 18 months has finally reaches the most frontal parts.

Jackson DE, et al says that 'Terminal myelination zones' are persistent hyperintensity regions on T2-w sequences [34] may be seen within the peritrigonal areas well into adulthood, & it is differentiated from white matter disease by seeing the presence of a rim of normal myelinated brain between these areas and the ventricular margin. (35)

FIGURE - 6



11-month-old boy imaged at 3 Tesla strength.

(A) Coronal T1-weighted image shows myelination of adult pattern with high signal myelin extending into the subcortical U fibers of the frontal, temporal lobes and cerebellum.

(B) Axial T2W FLAIR image shows low signal myelin in the deep white matter of the anteromedial occipital lobes seen on the right (arrow).

(C) Axial T2-W (FSE-IR) image shows low signal myelin in the deep white matter of the cerebellar hemispheres.

(D) Axial T2-W FSE-IR image at a superior level shows hypointense myelination of the occipital subcortical U-fibers. Low-signal myelin is seen in the deep temporal white matter and the subcortical white matter of the temporal lobes shows high signal persistently.

TABLE - 2

Age specific progression on myelination [36,37,38,39]

Age Specific Progression of Myelination on MRI				
Age (Months)	T1 (Signal)	T2 (Signal)	T2 FLAIR (Signal)	DTI (Anisotropy)
Birth	Medulla ↑ Dorsal pons ↑ Brachium pontis ↑ I/S CBL peduncles ↑ Midbrain ↑ VL Thalamus↑ Posterior limb IC↑ Perirolandic centrum semiovale and gyri↑ Optic nerves, tracts, and radiations↑	Medulla ↓ Dorsal pons ↓ Midbrain ↓ Perirolandic gyri↓ I/S CBL peduncles↓ VL Thalamus ↓	Deep occipital WM ↓ Deep frontal WM ↓ Deep temporal WM ↓	Central WM tracts↑ Peripheral WM ↓ All CBL peduncles↑ ML and MLF↑ Corticospinal tracts↑ Cerebral peduncles↑ IC and corona radiata↑ Cingulum↑, Fornix ↑ Corpus callosum↑ Anterior commissure ↑, UF↑
2	Deep cerebellar WM↑ Anterior limb IC↑	Brachium pontis ↓ Posterior limb IC ↓ Perirolandic centrum semiovale ↓ Optic tracts↓	Deep occipital WM ↑ Deep frontal WM ↑ Deep temporal WM ↑	FA in peripheral white matter dramatically increasing
4	Entire cerebellum↑ CC (splenium) ↑	Optic radiations↓ Calcarine fissure ↓	Dorsal pons ↓ Brachium pontis ↓ Posterior limb IC ↓	Peripheral WM ↑ IFOF ↑ ILF ↑ Subcortical U-fibers↑ Forceps minor ↑ Forceps major ↑ (inverted V shape)
6	CC (entire) ↑	CC (splenium) ↓ Ventral pons ↓	Optic radiations ↓ Perirolandic centrum semiovale↓ CC (entire) ↓	Increasing definition of forceps major and forceps minor
8	Subcortical U-fibers occipital ↑	Anterior limb IC ↓ CC (entire) ↓	Anterior limb IC ↓	Forceps major obtaining inverted U shape
12	Subcortical U-fibers frontal and temporal↑ Brain achieves adult appearance on T1.	Deep WM cerebellum↓ Early occipital subcortical U-fibers ↓ Temporal central WM↓	Deep occipital WM ↓	SLF↑ Fiber crossing areas ↑
18	Minimal change	Subcortical U-fibers occipital poles↓ Entire posterior fossa↓	Deep frontal WM ↓ Subcortical occipital WM ↓	Increasing FA and tract thickness throughout brain
24	Minimal change	Subcortical U-fibers frontal and temporal poles↓	Deep temporal WM ↓ Subcortical frontal WM↓	Increasing FA and tract thickness throughout brain
Other	T1 provides little information after 1st year of life.	Periatrial terminal zones may remain hyperintense into 2nd decade.	Subcortical U-fibers in temporal poles remain hyperintense after 24 months.	FA color maps achieve adult appearance by 48 months.

DIFFUSION TENSOR IMAGING (DTI)

Molko N, et al.says that **Diffusion tensor imaging (DTI),** a new MRI technique which measures the Brownian motion of water molecules in tissue.[40] The microscopic length scale and orientation information are the two aspects of DTI which makes it very powerful. The microscopic length scale of water diffusion in tissue imparts microscopic spatial sensitivity to DTI, while the orientation information is used in distinguishing homogenous white matter on conventional MRI into its constituent fiber tractsas says by **Seidenwurm D, et al** (41)

Tamagawa Y, et al.says that now , newer techniques like DWI and DTI prove to be more sensitive than conventional MRI for assessment of brain development and white matter (WM) fibers density and maturation.[3],[42],[43] Tractography is performed in DTI and in colored 3D shape, the findings are expressed. Free diffusion of water occurs equally in all directions in normal brain which is known as “isotropic” diffusion. “Anisotropic” diffusion is said to occur If the water diffuses in a medium with barriers and the diffusion becomes uneven.

There are several ways to measure anisotrophy , one among which is fractional anisotropy (FA). Fractional anisotropy (FA) is a scalar value between zero and one. A value of zero means that diffusion is isotropic, i.e. it is unrestricted. A value of one means that diffusion occurs only along one axis and is fully restricted along all other directions.

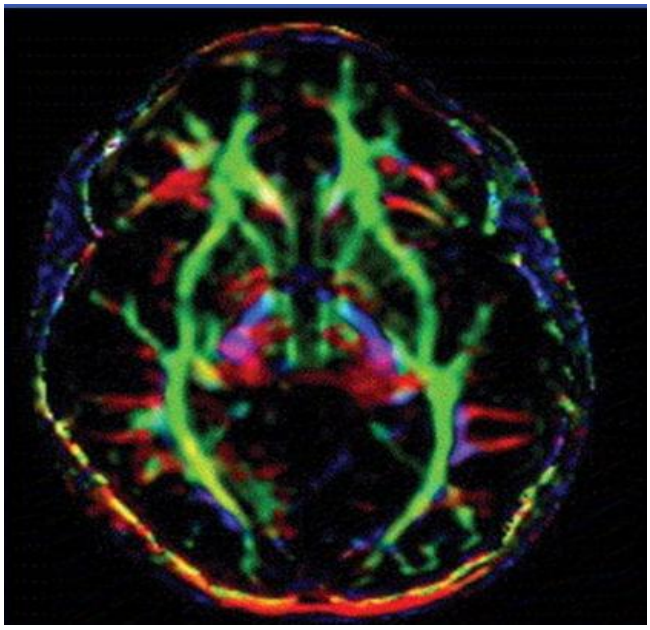
Mild injury leads predominantly to WM damage while severe brain injury results in tissue loss and necrosis in both WM and gray matter. Selective WM damage in mild hypoxia-ischemia can be due to apoptosis of immature oligodendrocyte and dysfunction of mature oligodendrocytes.[44,45,46] In era of advanced medical care at-risk neonates, more and more children survive.

Hence it is important to assess, soon after birth, the prognosis of children with hypoxic-ischemic encephalopathy. CT, USG, and conventional MRI can predict brain injury, but cannot quantify white matter damage. Infants with brain injury and those without brain injury can be detected by DTI using fractional anisotropy, voxel volume, and number of fiber bundles.

The correlation between fractional anisotropy values in the posterior limbs of the internal capsule correlates very well with neonatal behavioral neurological assessment scores. DTI can quantify white matter injury in neonates with HIE [47].

COLOUR CODED FA MAP

FIGURE - 7



Colour coding of the diffusion data according to the principal direction of diffusion

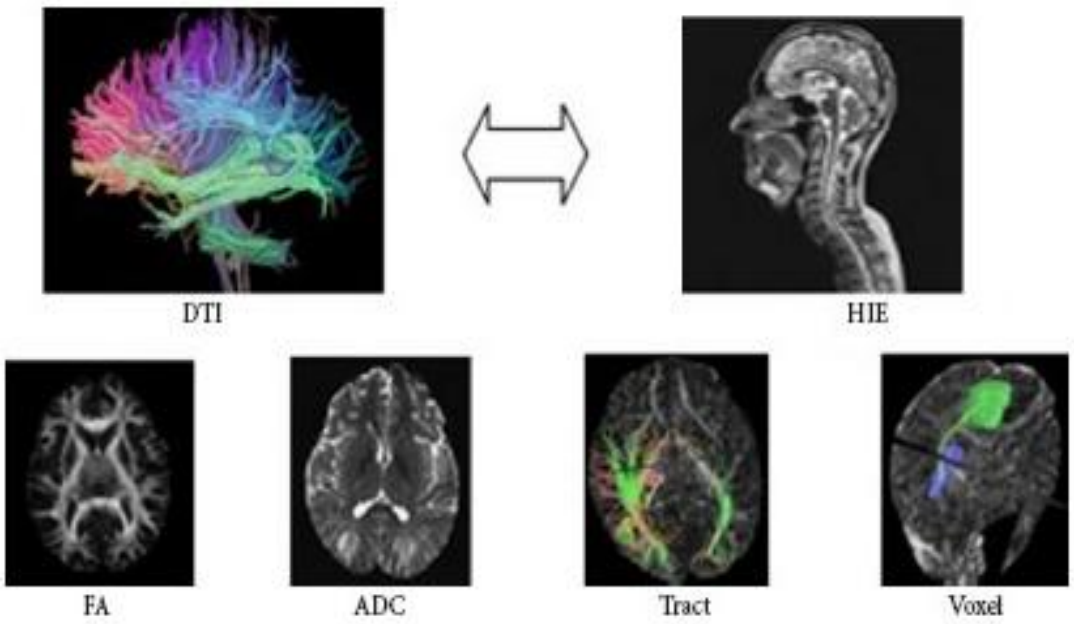
Red – transverse axis

Blue- superior to inferior

Green- anterior to posterior

Intensity of the colour is proportional to the fractional anisotrophy

FIGURE – 8



DTI parameters demonstrates brain white matter injury of neonates quantitatively. FA values and voxel numbers of region of interest are better than ADC values in estimating white matter injury.[48]

In preterm neonates hypoxic ischemia can damage the white matter, mainly around the cerebral ventricles.As the volume of blood in vessels flowing towards the ventricle is only a quarter of that flowing towards grey matter, hypoxia can easily damage the brain tissue. In neonates born at 34 weeks oligodendrocytes are in the period of high differentiation and are susceptible to injury [49].

Grunau RE, et al says that The two important causes of neonatal brain paralysis and mental retardation are corticospinal tract traveling through the regions around the ventricle, and easy damage of motor function [50].

Gojnic M, et al says that yearly around 1.2 million neonates are born with hypoxic-ischemic brain damage & 1 million of them end up with permanent CNS dysfunction. [51]. Early diagnosis and treatment is of at most importance in preventing irreversible brain damage.

The only non-invasive technology available to study the cerebral white matter fibres in neonates with damaged white matter of the brain is DTI . It visualises abnormalities of white matter fibre bundles caused by hypoxic ischemia, such as breakage, rarefaction, and damage, and shows the running, circumventing, and crossing of cerebral white matter fibre bundles [52].

With DTI, fractional anisotropy of brain-water diffusion can be quantified and maturation of the myelin sheath of brain white matter fibre bundles can be assessed by changes in ADC and FA. DTI can help in early treatment of neonates with brain damage.

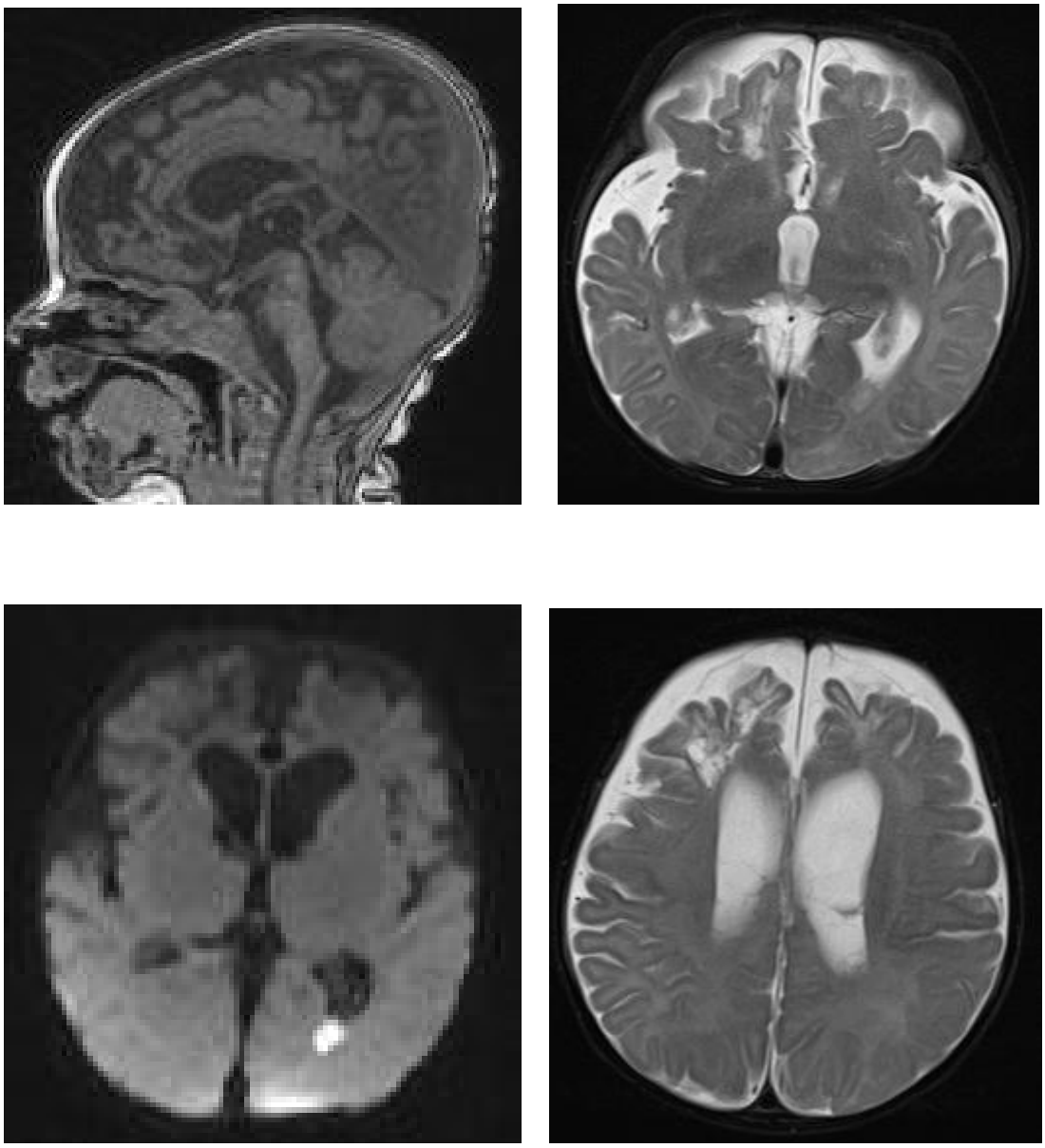
Neonatal cerebral white matter (WM) is susceptible to a number of perinatal insults such as hypoxic–ischemic encephalopathy (HIE), sepsis, hypotension, and prematurity(53). The areas that are most vulnerable to HIE are basal ganglia, thalami, hippocampi, and perirolandic gray matter & WM (54)

Neonatal MRI predicts the outcomes following HIE with injury to the basal ganglia and thalamus and perirolandic regions are highly predictive of motor dysfunction [55]. If there is no injury to the central gray nuclei and to watershed regions then there will be normal motor development.

Hawgood S, et al. and Kjaer MS, et al Says that Extracorporeal membrane oxygenation (ECMO) can also cause neonatal white matter injury, [57](58) So there is a need for a more advanced technique which is more sensitive to detect the white matter injury like DTI.The aim of this study was to detect the sensitivity of DTI in survivors of neonatal HIE .(59)

FIGURE - 9

BABY WITH HIE STAGE 3, MRI BRAIN



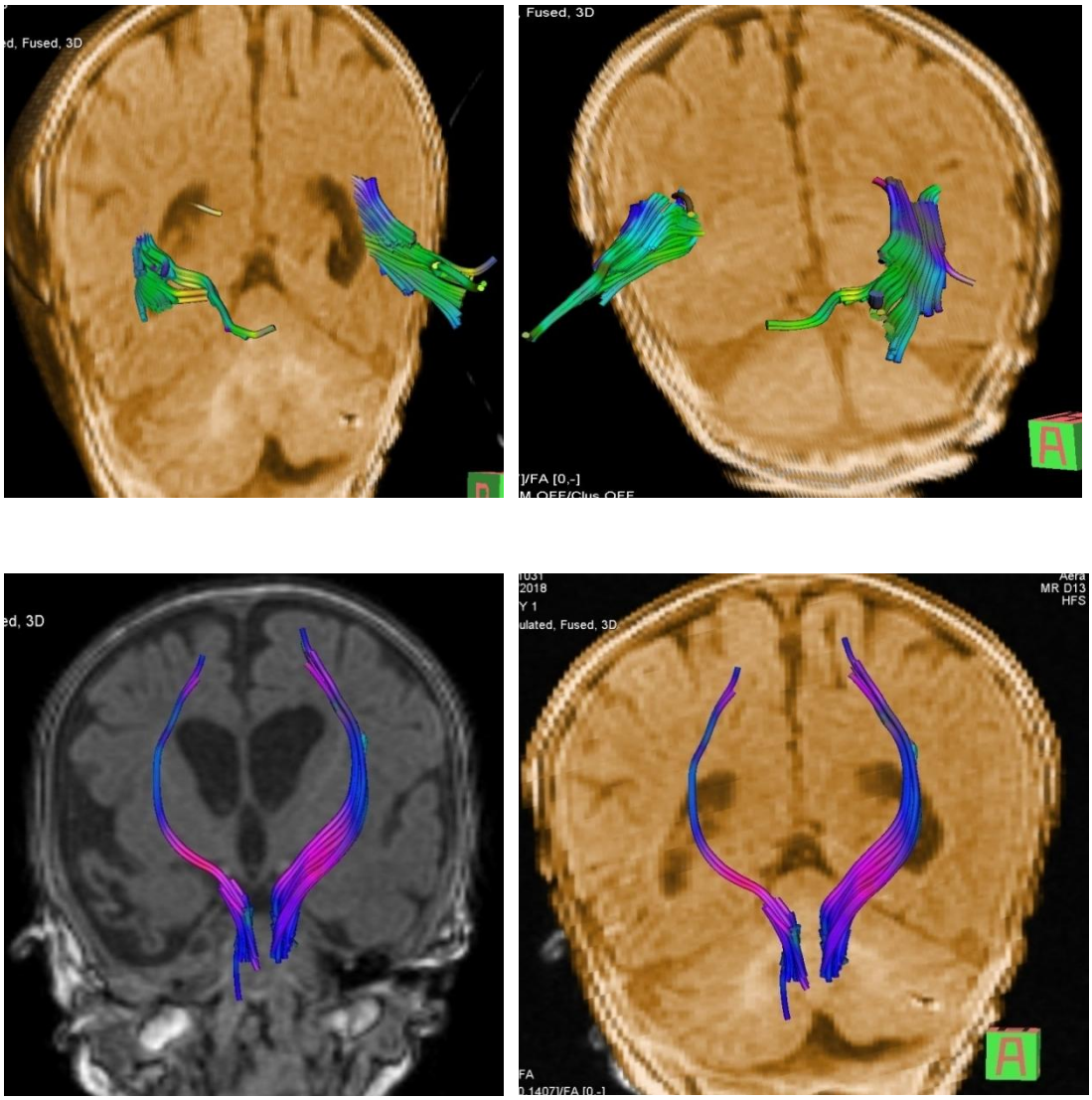
Gliosis in bilateral frontal and right temporal region

Diffusion restriction noted in occipital horn of left lateral ventricle.

Multiple small chronic infarcts in bilateral centrum semiovale and corona radiate.

FIGURE - 10

BABY WITH HIE STAGE 3, DTI WITH TRACTOGRAPHY



DTI with Tractography shows,

Thinned out left cortico spinal tract compare to the right

Thinned out left inferior longitudional fasciculus compare to the right side.

DENVER DEVELOPMENTAL SCREENING TEST

For examining children 0-6 years of age as to their developmental progress.[60]

Important Milestones:[61]

TABLE 3

MILESTONE ACHIEVEMENT BY THE END OF 3 MONTHS

Social and Emotional	MOTOR	SENSORY
• social smile • Enjoys playing with other people • more expressive and communicates more with face and body • shows movements and facial expressions	• lies on stomach & Raises head and chest • lying on stomach & supports upper body with arms • lying on stomach or back & stretches legs out and kicks • Opens and closes hands • Brings mouth to hand • Grasps and shakes hand toys	• Closely watches faces • Follows moving objects • Recognizes familiar objects and people at a distance • Starts using hands and eyes in coordination • Smiles at the sound • Begins to babble • Begins to imitate some sounds • Turns head towards of sound

TABLE 4

MILESTONE ACHIEVEMENT BY THE END OF 7 MONTHS

Social And Emotional	MOTOR	SENSORY
• Enjoys play • sees in mirror images	• Rolls both ways • Sits with & without, support • Stands on leg. • Reaches with one hand • hand to hand object transfer.	• Joy is expressed using noise. • Babbles • full colour vision developed • maturation of distant vision • Improved steropsis

TABLE 5

MILESTONE ACHIEVEMENT BY THE END OF 12 MONTHS

Social and Emotional	MOTOR	SENSORY
• Stranger anxiety • parent anxiety • Role play • selective receptivity • Fearful • Prefers mother over father • attention seeking. • Finger sucking	• sits without support • Crawls • Creeps • sitting to crawling • Pulls up to stand • Walks with support • Stands without support • pincer grasp • two objects are banged together • Takes objects out of container	• Speech attention • obeys simple verbal commands • Babbles • Says "mama" & dada • hidden objects are found • identify picture • gesture Imitatation

AIMS AND OBJECTIVES

To correlate MRI brain findings and DTI findings in early neonatal period of term and preterm neonates with hypoxic ischemic encephalopathy and its clinical outcome.

DTI is currently the only way to quantify the maturation and damage of brain development in preterm neonates.

In the early stage, it can identify damages that cannot be screened by MRI.

It can provide evidence for developing effective measured of prevention, protection and rehabilitation for damage to the brain.

MATERIALS AND METHODS

Study Design: Prospective Study

Data Collection: Newborn babies with APGAR score of less than 7 with history of birth asphyxia referred for MRI to our department.

Study Centre: Department of Radiodiagnosis, Govt. Royapettah hospital and Kilpauk Medical College Hospital. Kilpauk,

Sample Size : 50

Duration of Study:1 Year and 3 months from July 2017 to September 2018

Statistical Analysis: Descriptive statistical analysis

Inclusion Criteria:

Term and preterm new born babies with APGAR SCORE of less than 7

Exclusion criteria:

New born with congenital anomalies

Syndromic babies

Infants with metabolic disorders

Associated hyperbilirubinemia

One time MRI & DTI images were taken with 1.5 Tesla GE superconductive magnet. All included babies were subjected to the study within 14 days of life. Prior written consent was obtained from all parents. Data collection was performed in the included study group using a proforma.

Proforma includes parents name , gestational age, date of birth , birth weight, term or preterm, day on which MRI was taken, mode of delivery, APGAR score, HIE stage, address, mobile number, findings in conventional MRI, findings in DTI and clinical assessment during serial follow up.

METHODOLOGY

The study was begun after obtaining institutional ethical committee clearance. All the included cases were subjected to imaging after obtaining written consent.

This study was conducted with full-term and preterm neonates with HIE (23 mild HIE cases , 16 moderate HIE cases and 11 severe HIE cases with a history of neonatal asphyxia) . The HIE patients were subdivided into mild, moderate and severe groups according to APGAR SCORE and sarnat and sarnat staging.Twenty newborn babies referred to MRI brain without abnormality were selected for control.

All 50 cases were subjected to conventional MRI and DTI within a maximum period of 14 days from birth. Babies attenders were well explained about the procedure and are advised to remove metallic pins, jewellery, hearing

aids and other metal objects outside the MRI gantry. Babies were positioned comfortably in supine position. Conventional MRI consisted of sagittal and axial T1-weighted and T2 -W ,diffusion weighted image and FLAIR imaging; DTI was acquired using single-shot Echo-planar imaging (EPI)

Imaging protocol

- T1 & T2 sequences in axial plane
- T1 W sequence in sagittal plane
- diffusion weighted imaging in axial plane
- A single-shot SE EPI was taken once with DTI.
- A cotton ball is stuck into each ear of patients to decrease the influence of noise
- Sedation if required
- Image acquisition is completed within 10 mins

Parameters set for T1

TR (repetition time): 400 – 620 ms

TE (echo time): 10 – 30 ms

Flip angle: 90 degrees

Slice Thickness – 3mm

Matrix – 288 x 160

Parameters set for T2

TR: 8000 – 9000 ms

TE: 80 – 120 ms

Flip angle: 90 degrees

Slice thickness 3 mm

FOV: 256 x 256mm

Matrix: 416 x 288

Parameters set for DT1

TR; - 12000

TE; - 96.4

Slice thickness; 3 mm

Flip angle - 90 degree

FOV; 128X 128mm b=1000s/mm

Matrix; 128 x 128

For each slice one image without diffusion weighting (b=0s/mm square) and six images with diffusion weighting (b=1000s/mm square) was obtained.

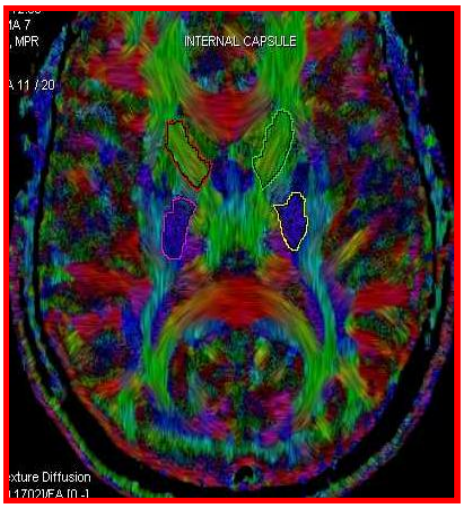
Post processing was done using automated GE software system. FA and ADC were measured in several ROI in brain including both thalamus ,corona radiata , anterior and posterior limb of internal capsule, SLF, and ILF.ROI were manually placed in FA map. According to anatomic structure and ADC map

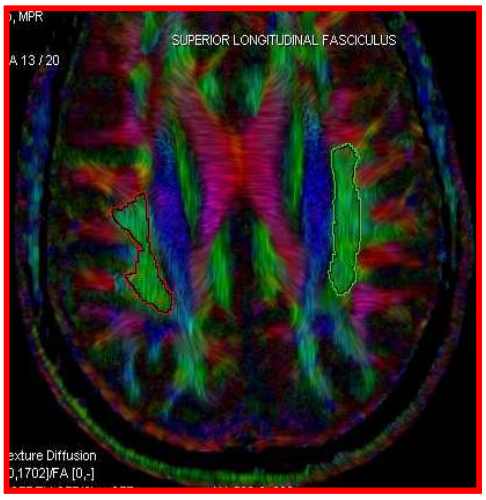
size of ROI was changed to cover all anatomical structure and to prevent mutual influence of volume effects between neighboring regions.

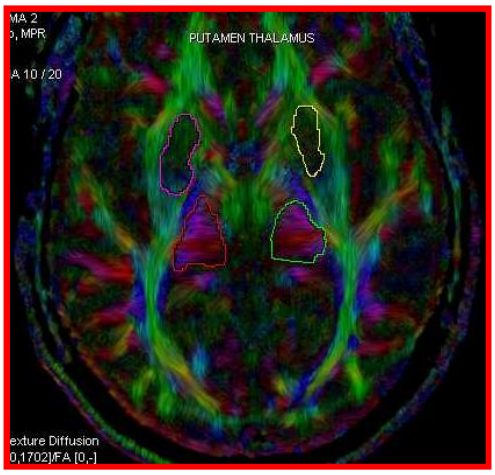
From our study in selected control babies we found mean FA value for corona radiate is 0.60 anterior limb of internal capsule is 0.60,posterior limb of internal capsule is 0.59,superior longitudinal fasiculus is 0.58, inferior longitudinal fasiculus is 0.54,and thalamus is 0.55.

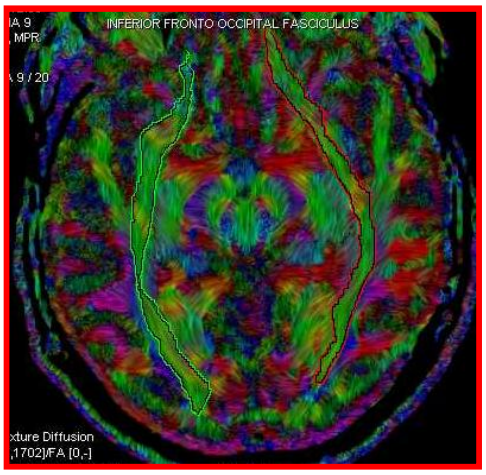
All babies were followed at 3 months interval for 1 year and developmental milestones were assessed using Denver Developmental scale.

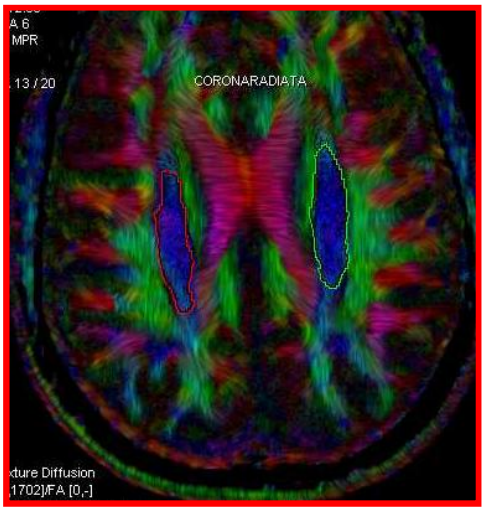
FIGURE - 11









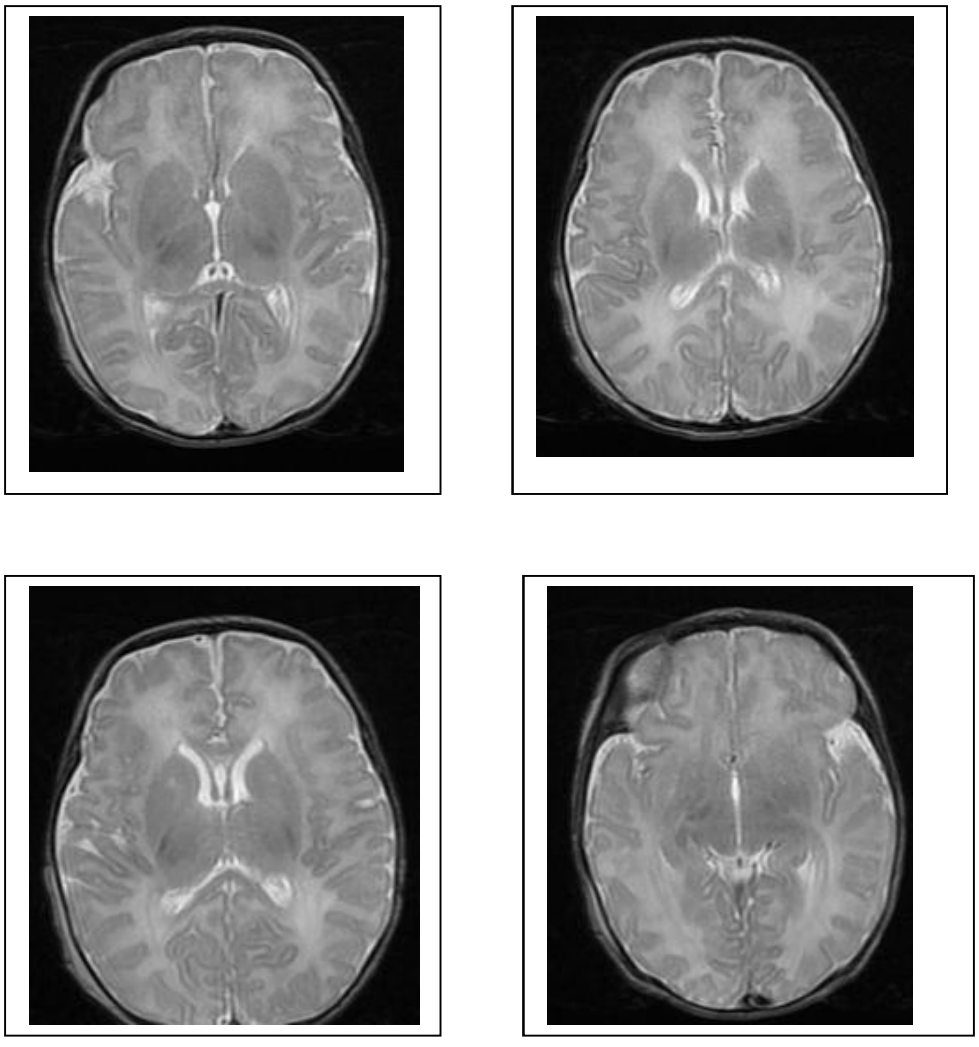


From controls ,FA value is calculated in thalamus,corona radiata, anterior and posterior limb of internal capsule, superior and inferior longitudinal fasiculus

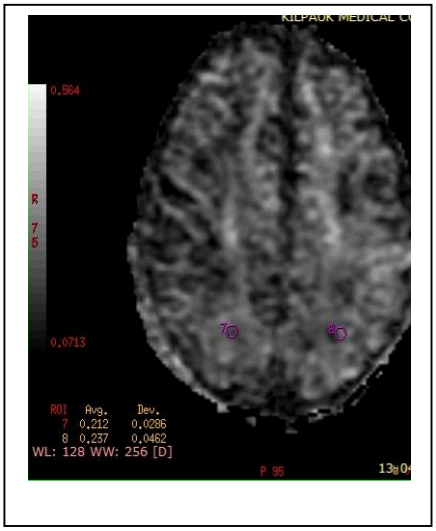
CASE 1

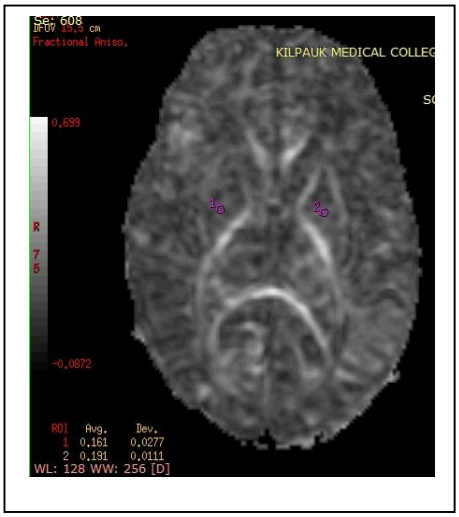
12 days old female baby presented with h/o birth asphyxia with APGAR score of 7 and HIE stage II There was no significant abnormality in conventional MRI sequences.

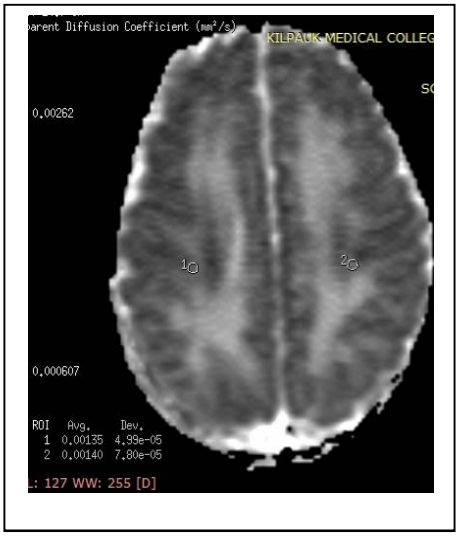
No significant difference in ADC value but DTI shows significant difference in FA value in anterior and posterior limb of internal capsule

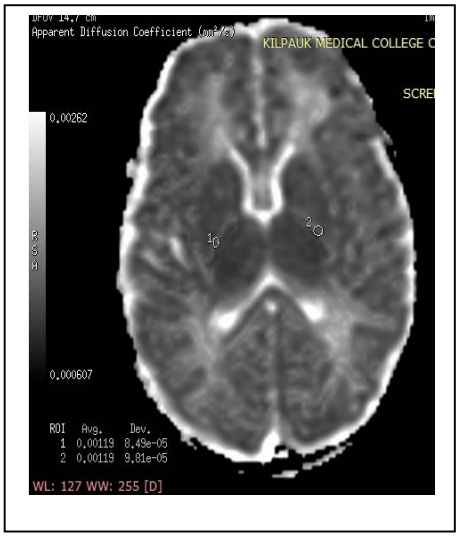


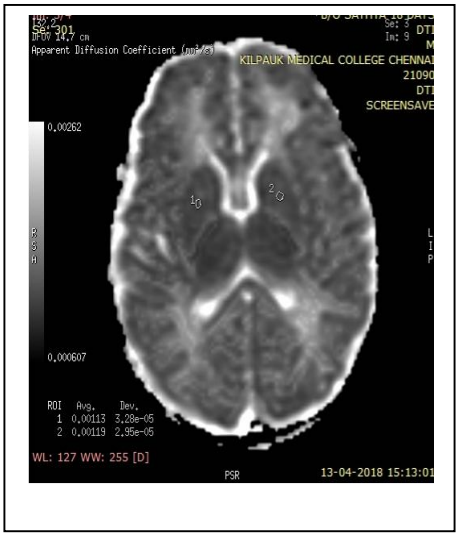
There was no significant abnormality in conventional MRI sequences.

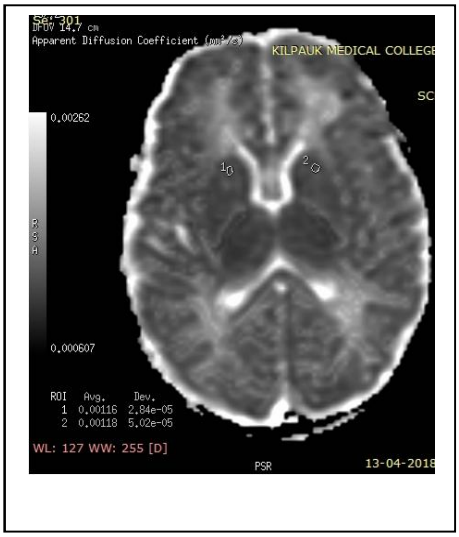




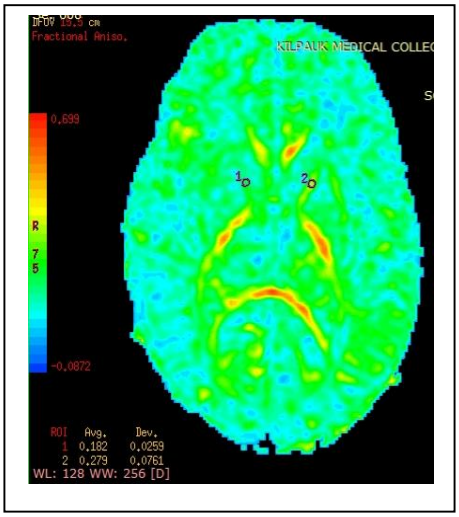


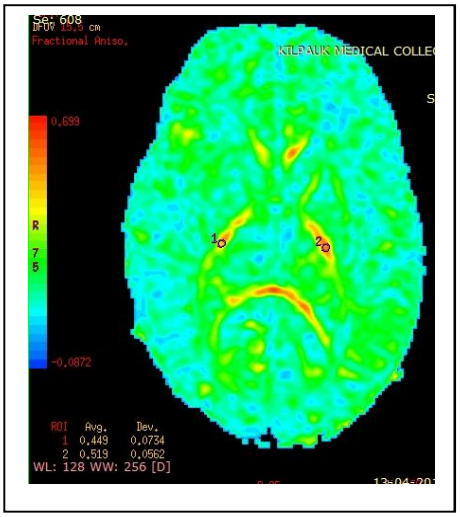


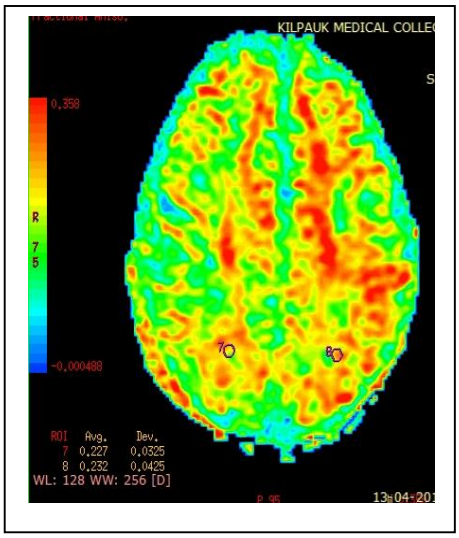


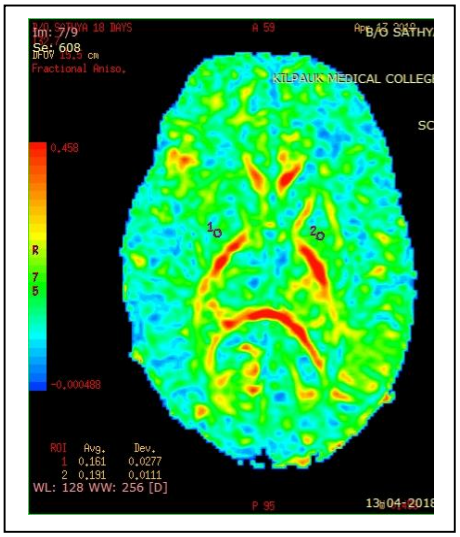


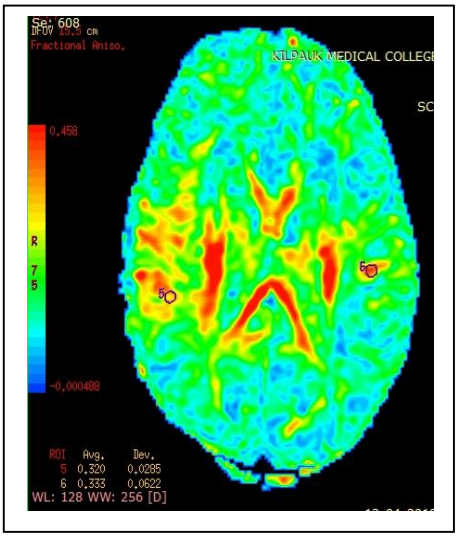
No significant difference in ADC value









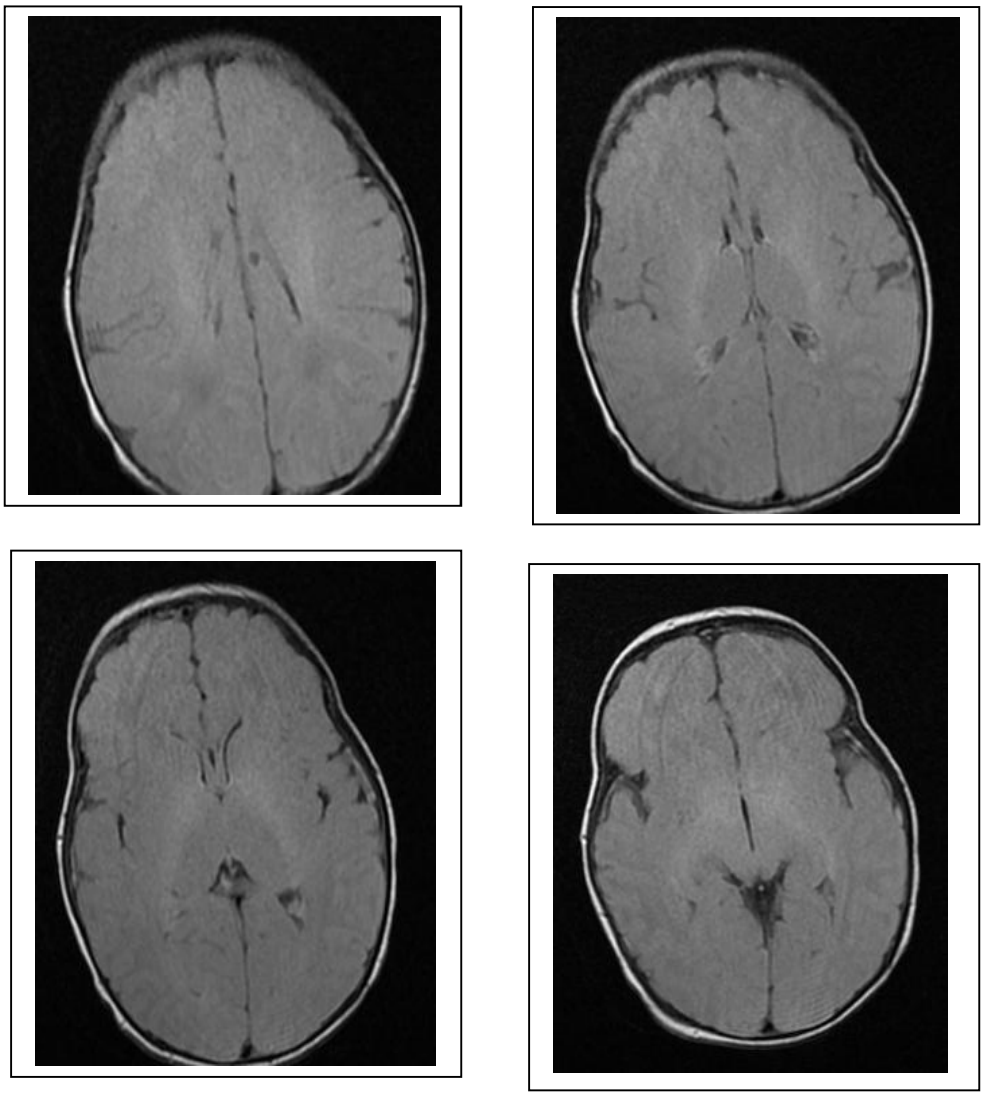


Shows significant difference in FA value in anterior and posterior limb of internal capsule.

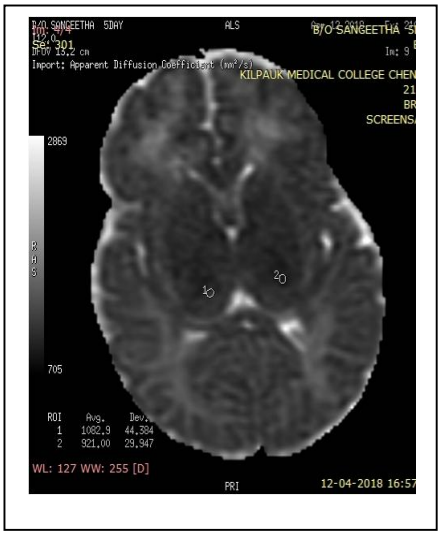
CASE 2

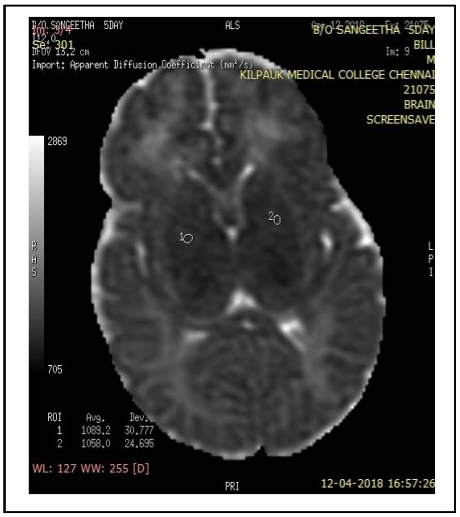
5 days old female baby presented with h/o birth asphyxia with APGAR score of 7 and HIE stage I. There was no significant abnormality in conventional MRI sequences.

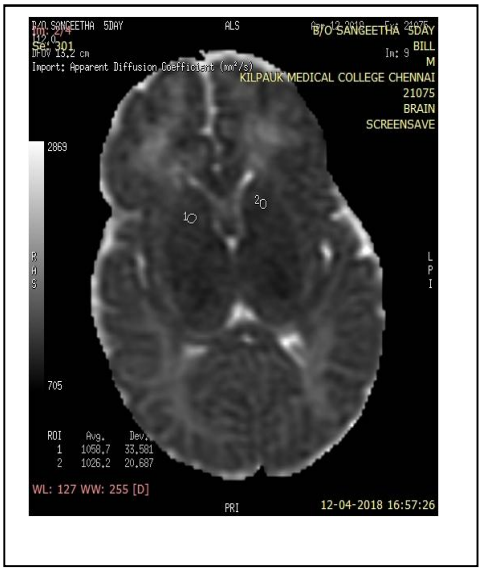
Significant difference in ADC value in posterior limb of internal capsule and DTI shows significant difference in FA value in posterior limb of internal capsule

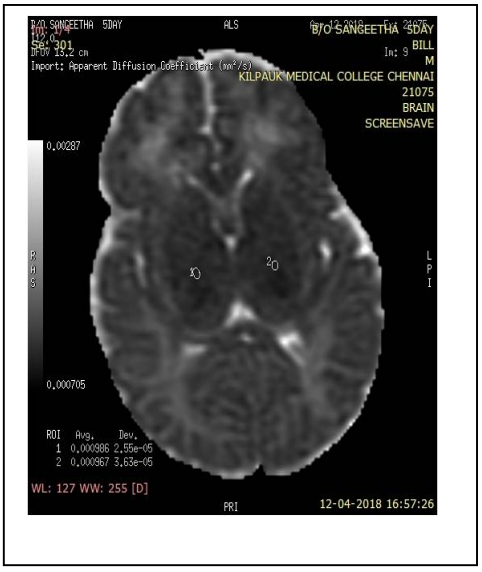


There was no significant abnormality in conventional MRI sequences.

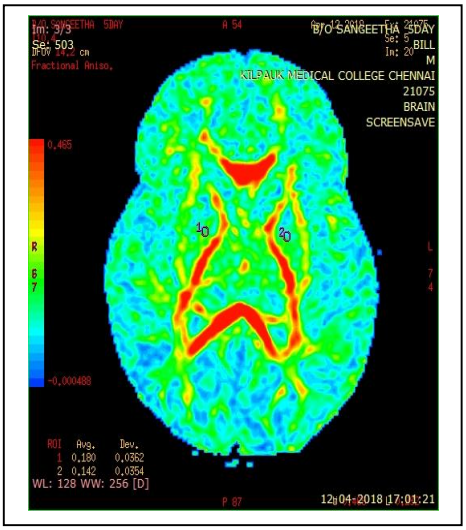


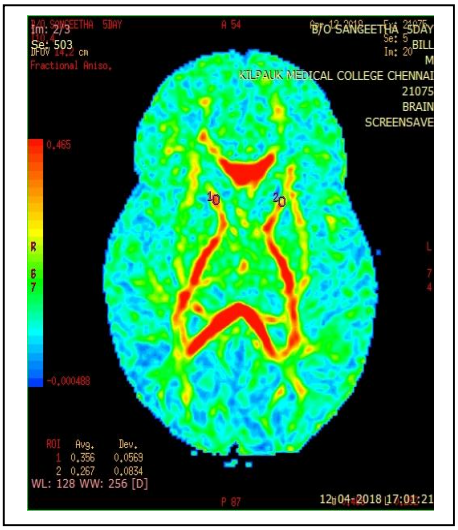


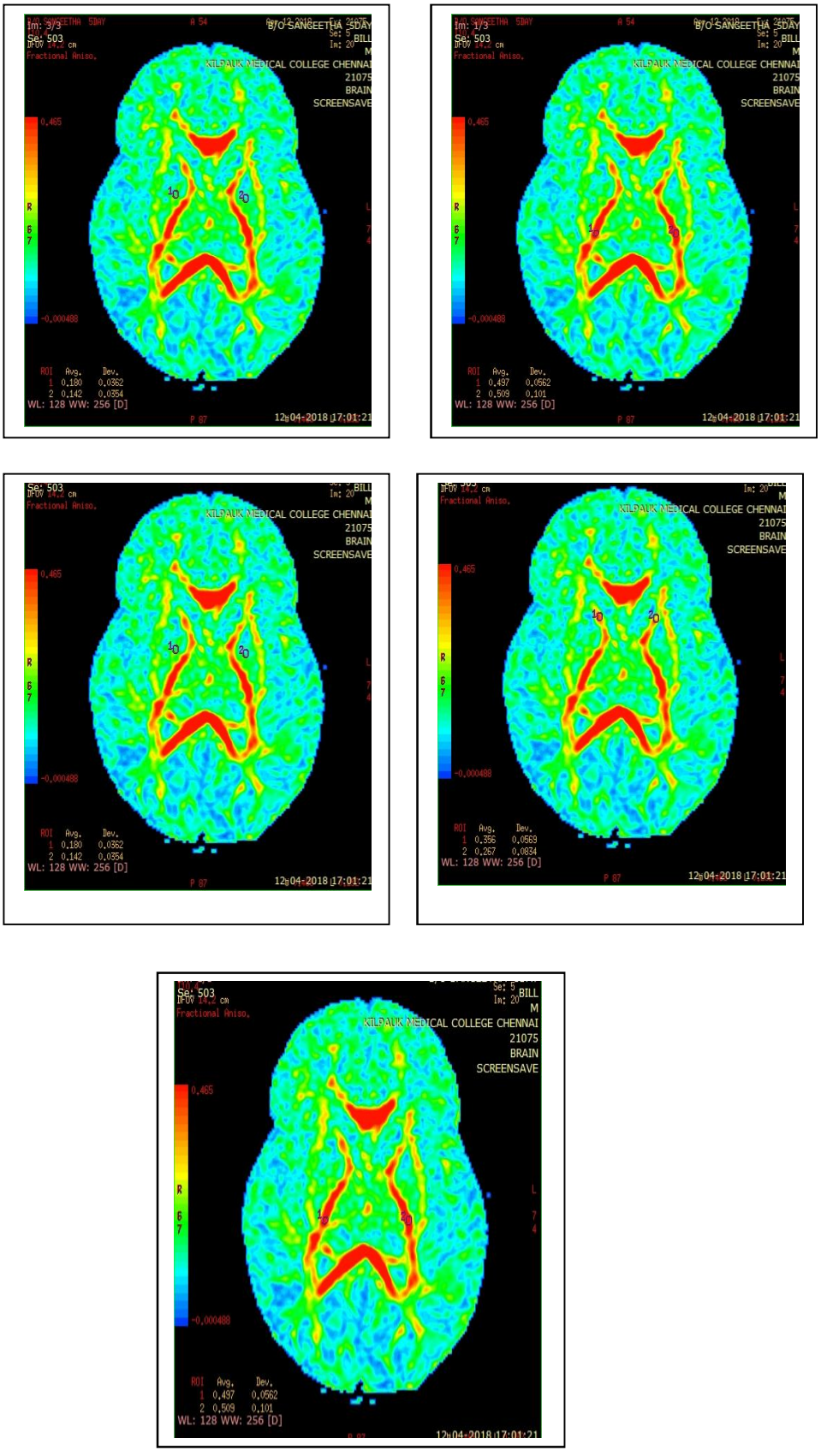




Significant difference in ADC value in posterior limb of internal capsule





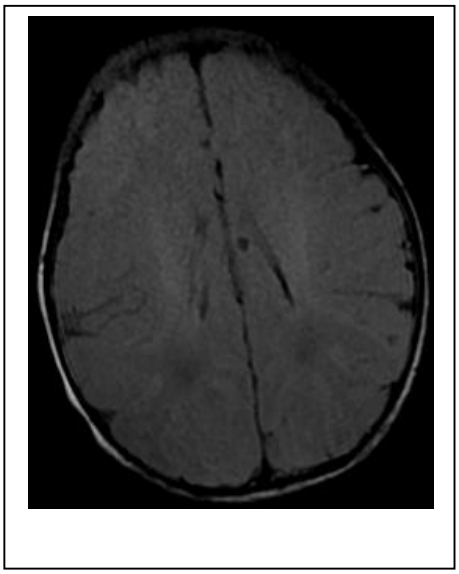


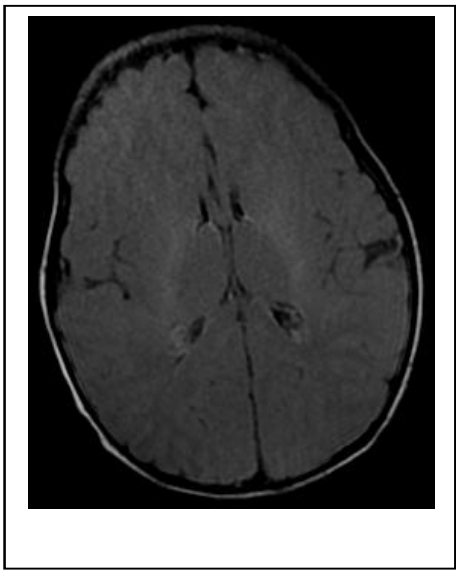
Significant difference in FA value in posterior limb of internal capsule

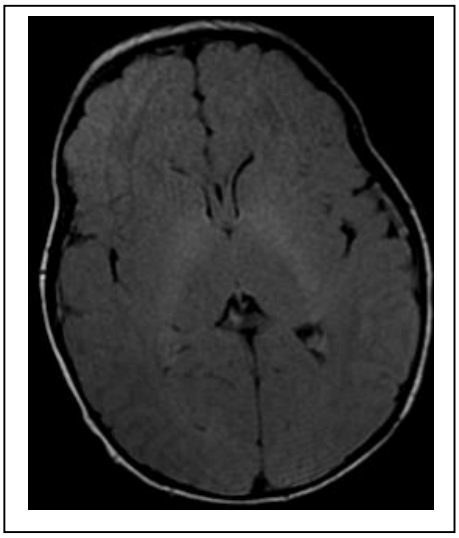
CASE 3

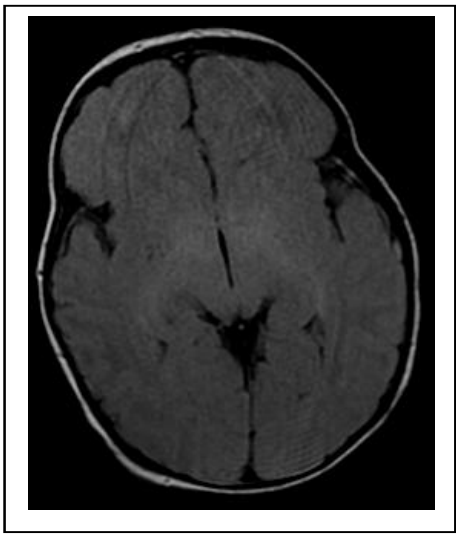
13 days old male baby presented with h/o birth asphyxia with APGAR score of 6 and HIE stage II.There was no significant abnormality in conventional MRI sequences.

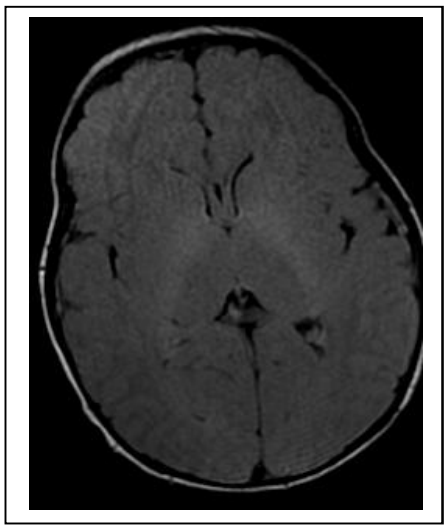
No significant difference in ADC value in posterior limb of internal capsule and DTI shows significant difference in FA value in anterior and posterior limb of internal capsule

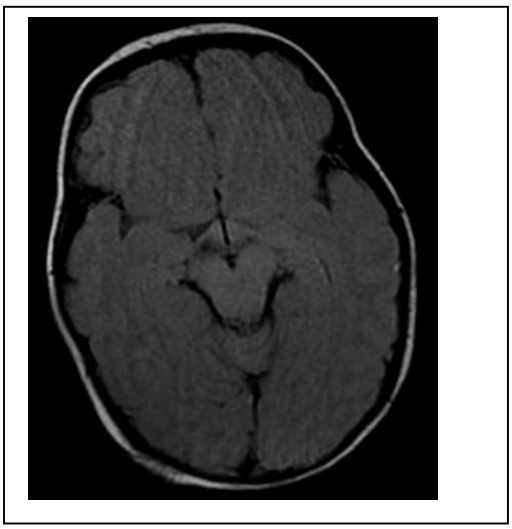




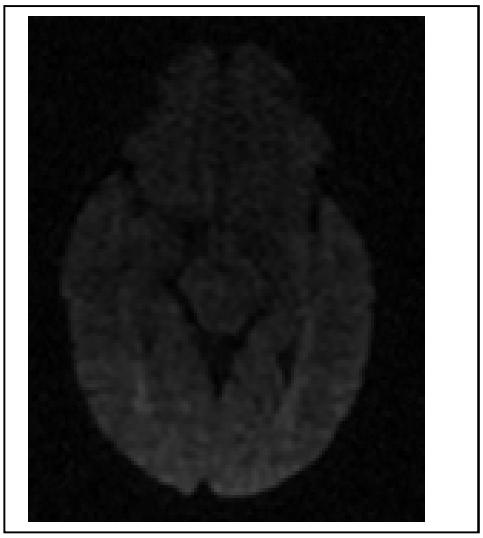


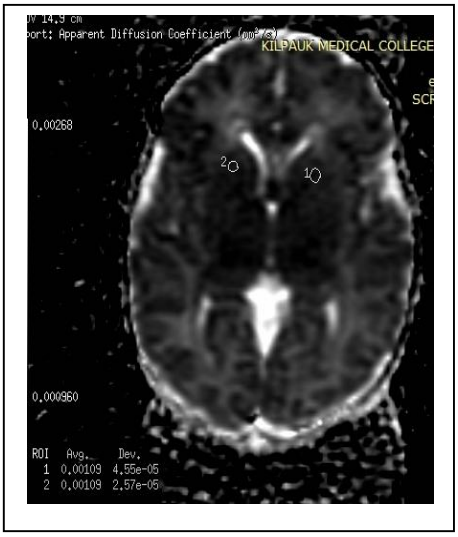




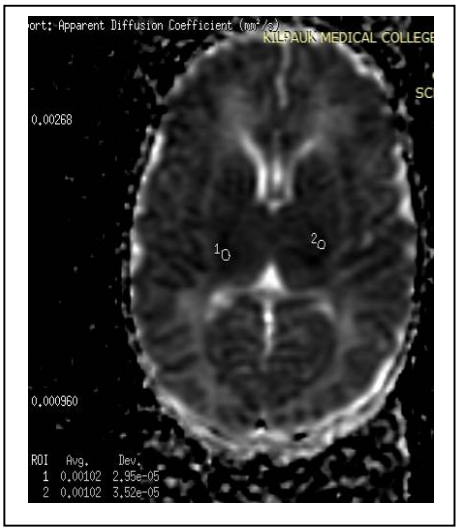


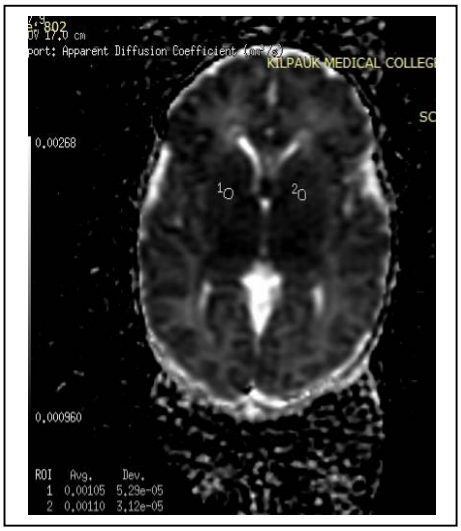
There was no significant abnormality in conventional MRI sequences.



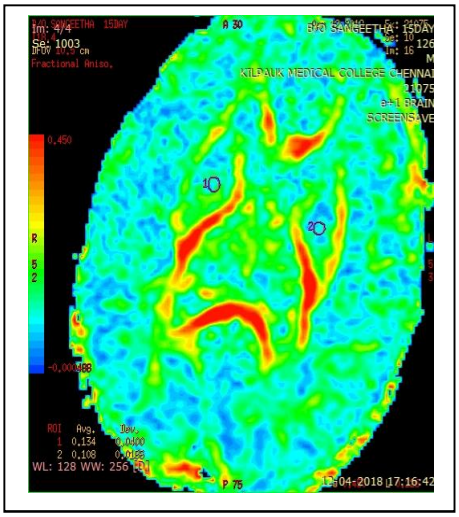


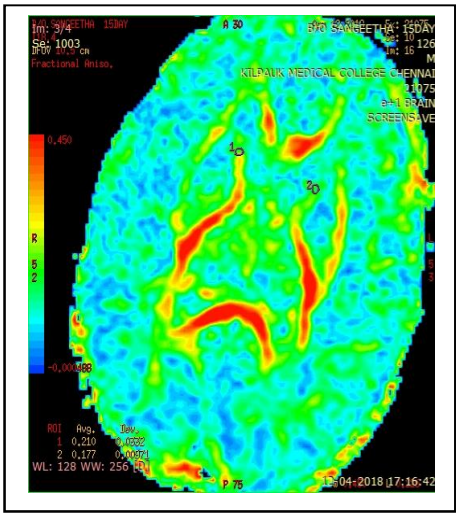
DWI shows no abnormality

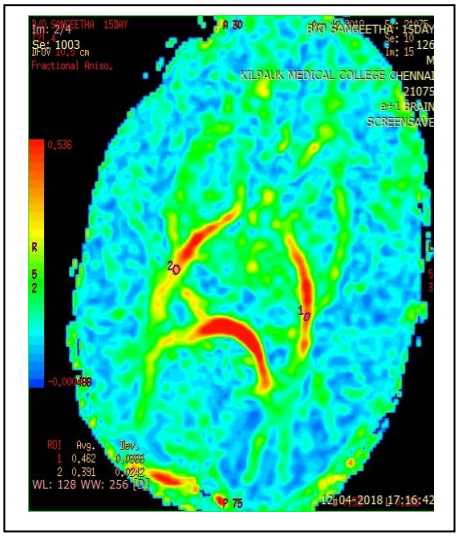


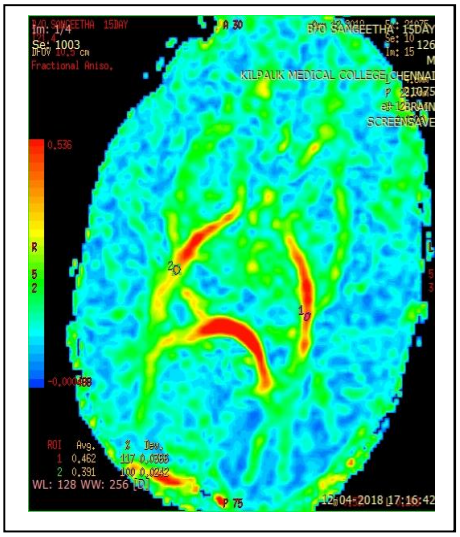


No significant difference in ADC value in posterior limb of internal capsule







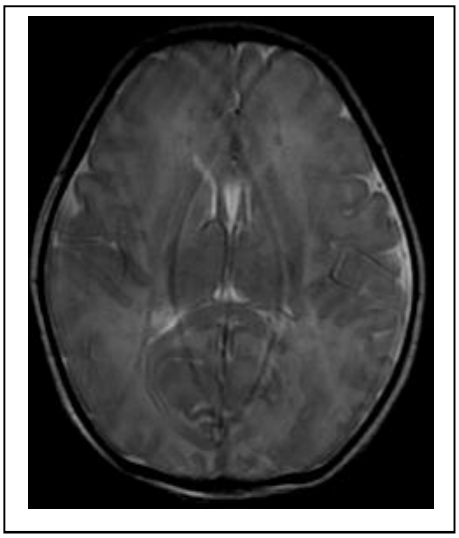


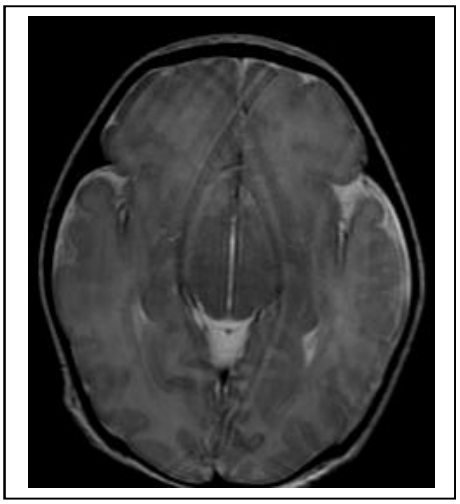
DTI shows significant difference in FA value in anterior and posterior limb of internal capsule

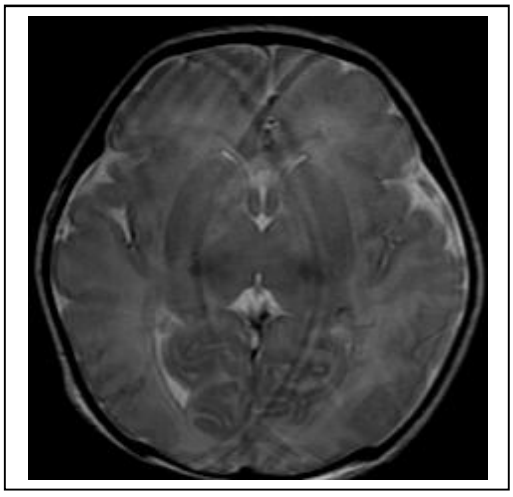
CASE 4

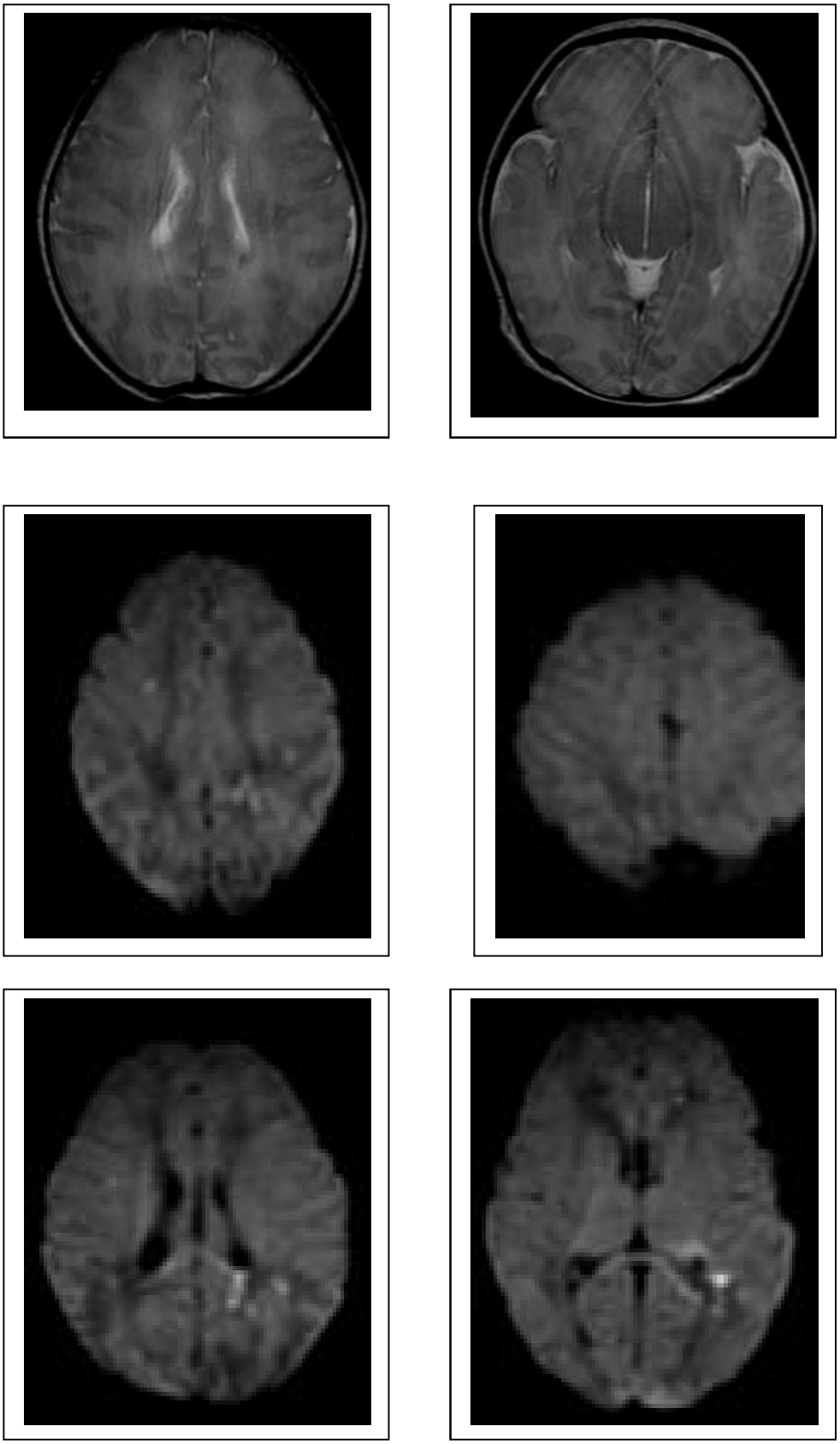
4 days old female baby presented with h/o birth asphyxia with APGAR score of 5 and HIE stage III There was diffusion restriction in left splenium of corpus callosum and left peritrigonal white matter in conventional MRI sequences.

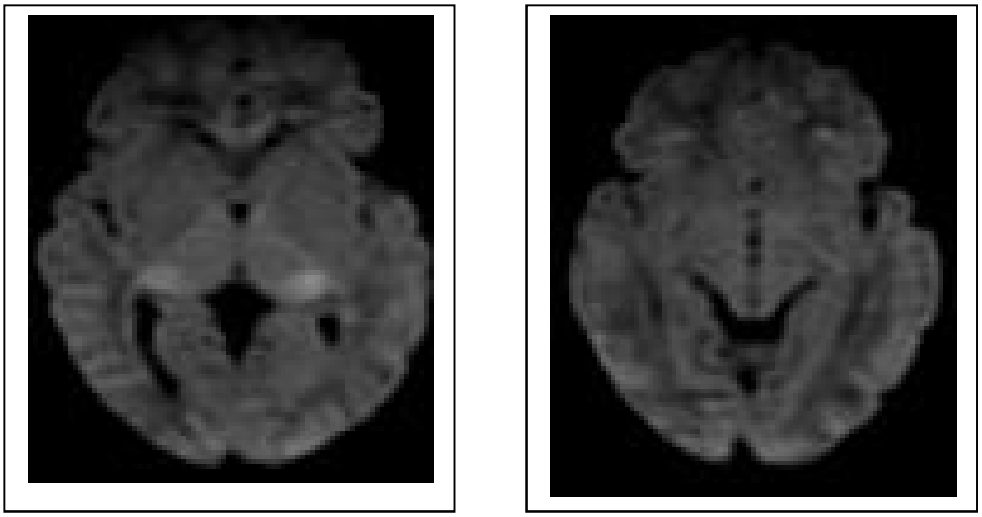
Significant difference in ADC value in posterior limb of internal capsule and DTI shows significant difference in FA value in posterior limb of internal capsule.



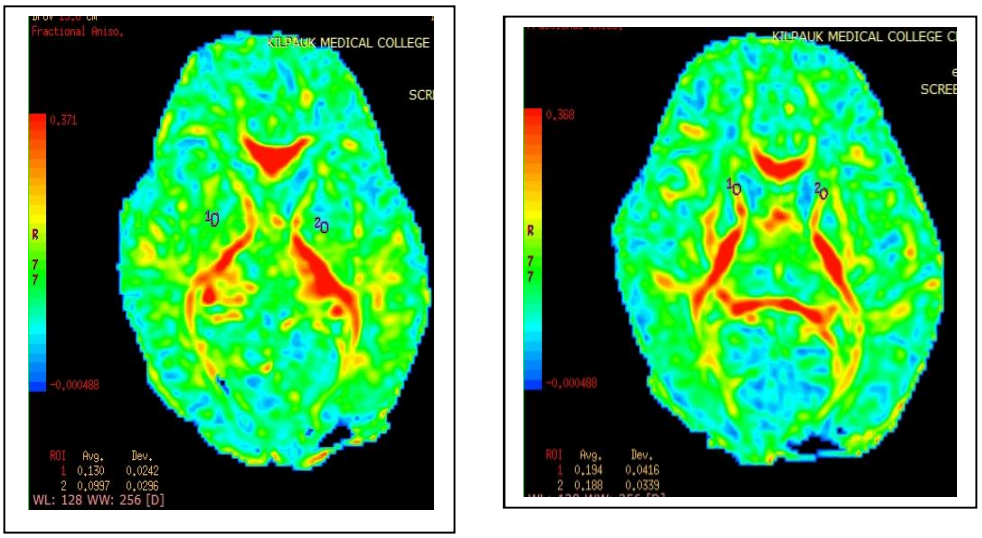


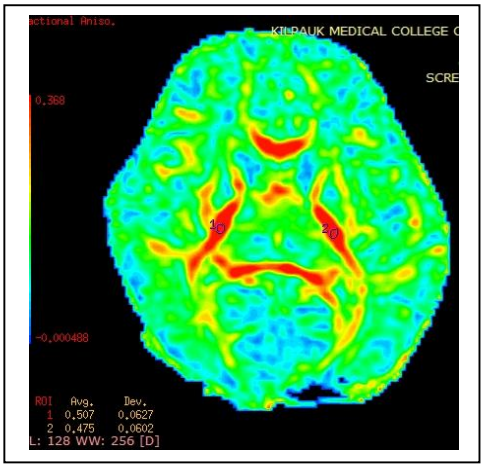






There was diffusion restriction in left splenium of corpus callosum and left peritrigonal white matter in conventional MRI sequences.





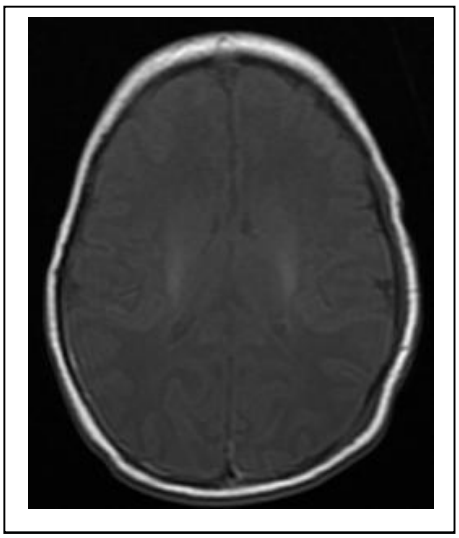
DTI shows significant difference in FA value in posterior limb of internal capsule.

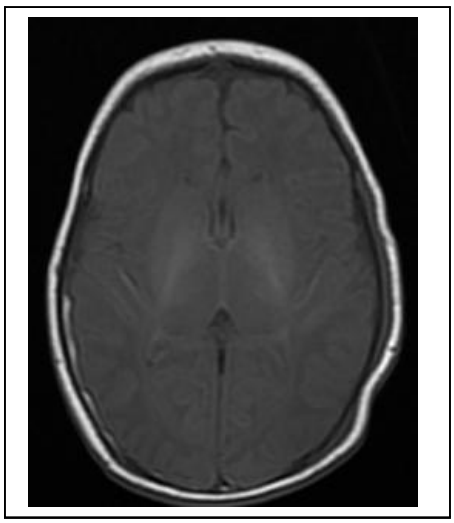
CASE 5

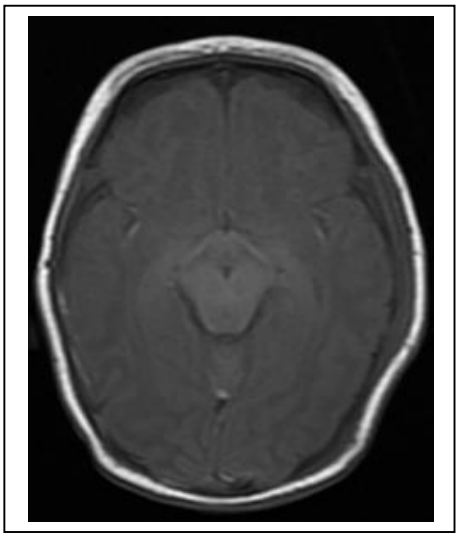
10days old male baby presented with h/o birth asphyxia with APGAR score of 6 and HIE stage I There was no significant abnormality in conventional MRI sequences.

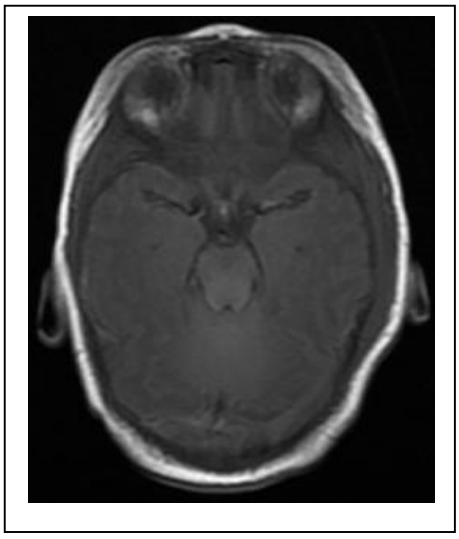
No significant difference in ADC value in posterior limb of internal capsule and DTI shows significant difference in FA value in posterior limb of internal c

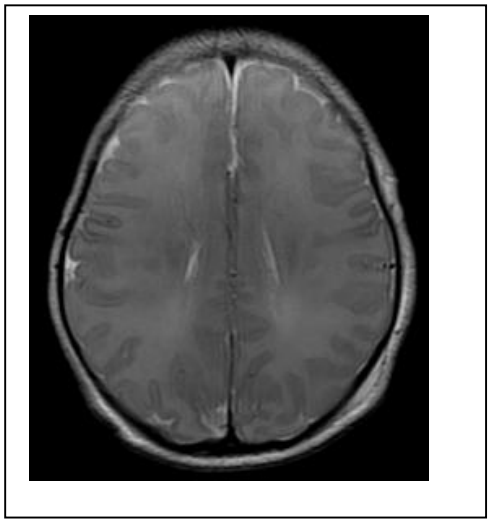
apsule

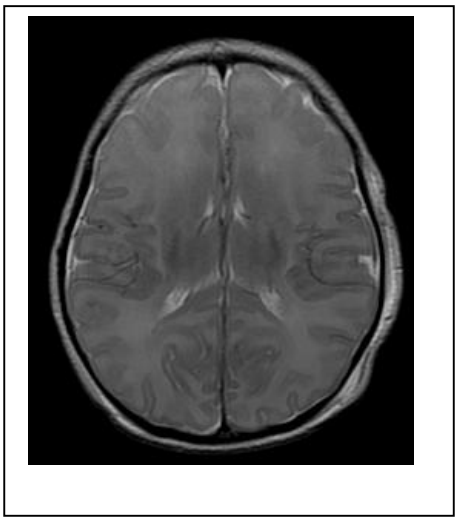


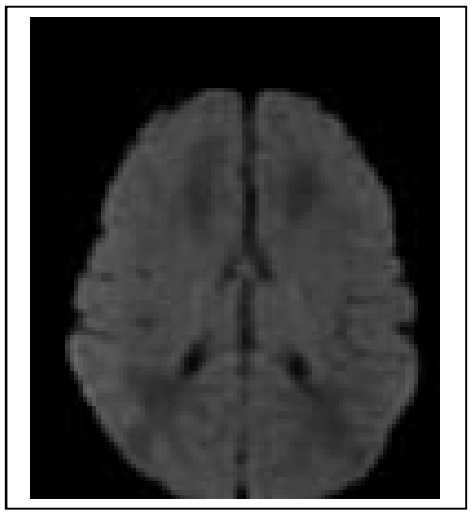


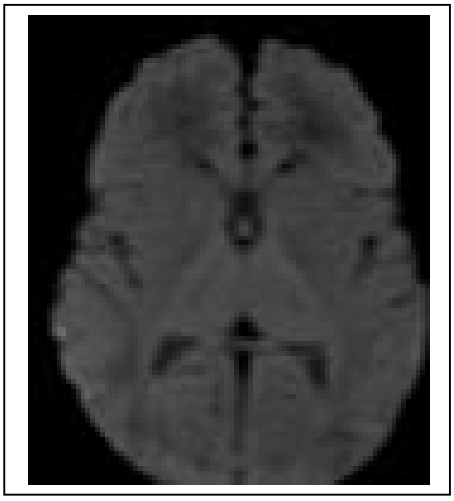


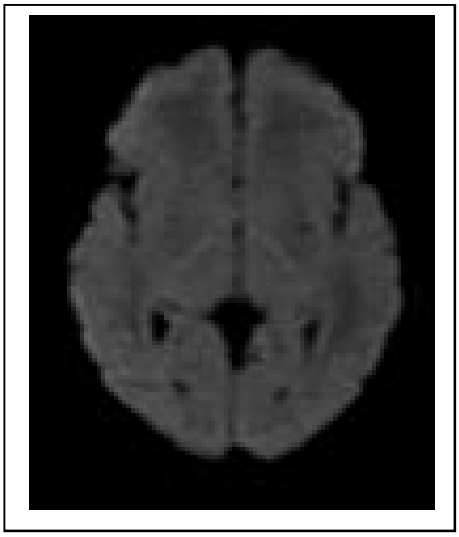




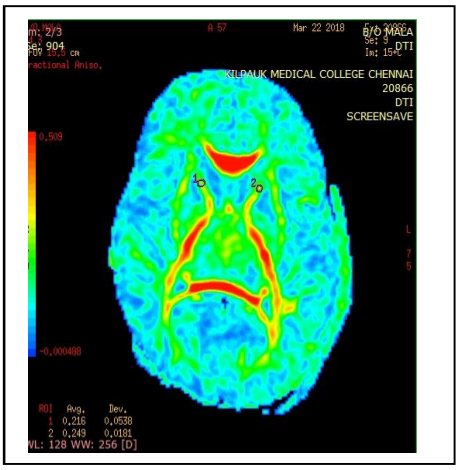








There was no significant abnormality in conventional MRI sequences.



DTI shows significant difference in FA value in posterior limb of internal capsule

STATISTICAL ANALYSIS AND RESULTS

The Data was entered in a excel worksheet and double checked. IBM SPSS version 22 software is used for statistical analysis.

Descriptive analysis:

Descriptive analysis was carried out using mean and standard deviation for quantitative variables.

The frequency and proportion are used for categorical variables.

Data was also represented using appropriate diagrams like bar diagram, pie diagram and box plots.

The sensitivity, specificity, positive and negative predictive values and diagnostic accuracy of the conventional MRI and DTI against gold standard – clinical outcome are computed and presented.

Reliability of the screening test is assessed by kappa statistics along with its 95% CI and P Value

P value < 0.05 is considered statistically significant.

TABLE 6

DESCRIPTIVE ANALYSIS OF CONTINUOUS VARIABLES.

	HIE 1	HIE 2	HIE 3
BIRTH WEIGHT			
<2.5KG	**6**	**7**	**2**
>2.5KG	**17**	**9**	**9**
GESTATIONAL AGE			
<32 WEEKS	**6**	**8**	**3**
>32 WEEKS	**17**	**8**	**8**
GENDER			
MALE	**17**	**9**	**8**
FEMALE	**6**	**7**	**3**
MODE OF DELIVERY			
NORMAL	**17**	**14**	**9**
LSCS	**6**	**2**	**2**
INVESTIGATION			
DTI	**19**	**16**	**11**
MRI	**7**	**6**	**11**
OUTCOME			
Developmental delay	**15**	**16**	**11**
Normal development	**8**	**0**	**0**

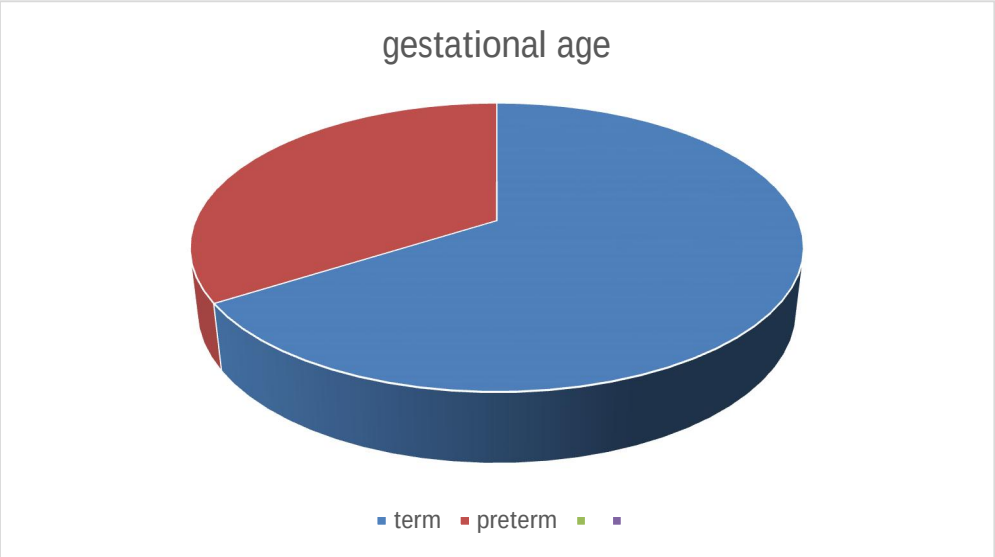
TABLE 7

DESCRIPTIVE ANALYSIS OF GESTATIONAL AGE

Term	**33**	**66%**
preterm	**17**	**34%**

FIGURE 12

PIE CHART SHOWING GESTATIONAL AGE DISTRIBUTION



In our study out of 50 babies 33 babies were term babies (66%) and 17 babies were preterm. (34%)

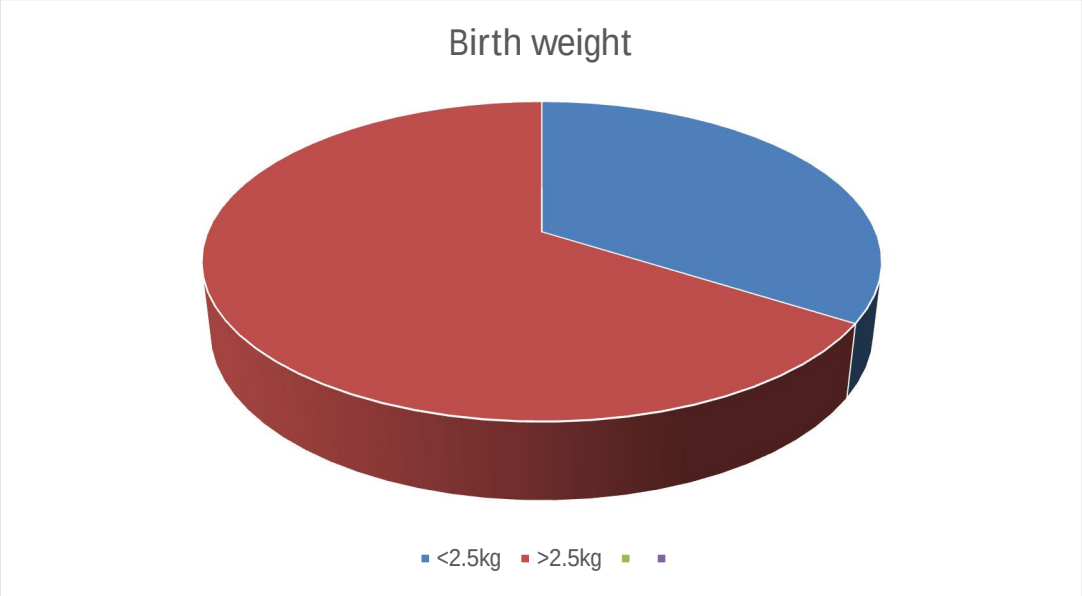
TABLE 8

DESCRIPTIVE ANALYSIS OF BIRTH WEIGHT

Birth weight <2.5 kg	Birth weight >2.5 kg
17	33
34%	66%

FIGURE 13

PIE CHART SHOWING DESCRIPTIVE ANALYSIS OF BIRTH WEIGHT



In our study out of 50 babies, 17 babies had weight less than 2.5kg (34%) and 33 babies were above 2.5kg (66%).

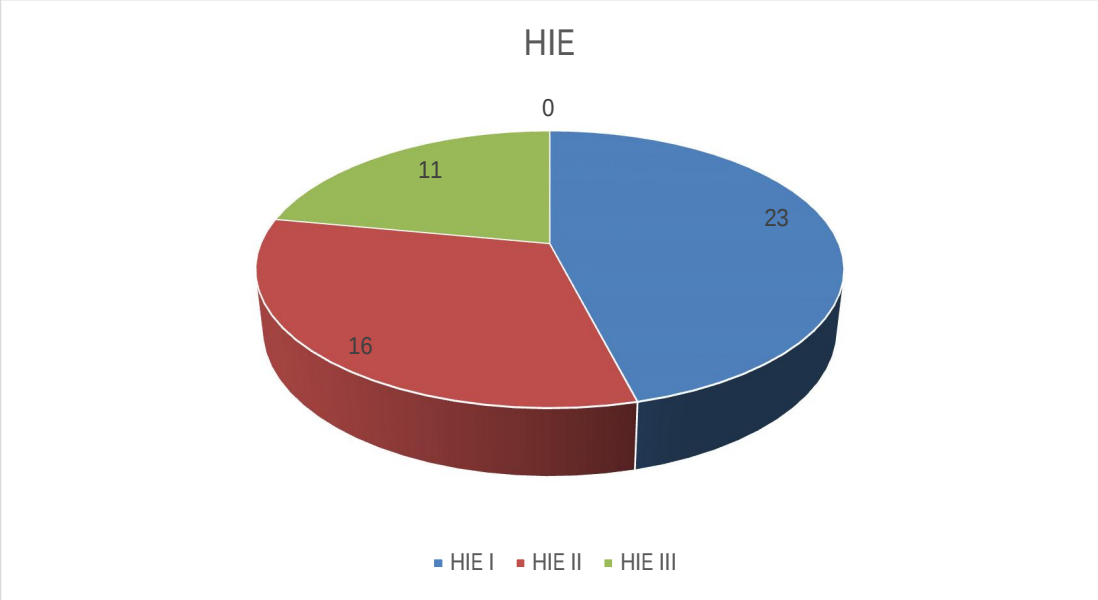
TABLE 9

DESCRIPTIVE ANALYSIS OF HYPOXIC INJURY BY SARNAT & SARNAT

HIE stage	No. of children	% of children
I	23	46%
II	16	32%
III	11	22%

FIGURE 14

PIE CHART SHOWING DISTRIBUTION OF HIE STAGES



In our study out of 50 babies, 23 babies belonged to HIE I (46%). 16 babies belongs to HIE II (32%) and 11 babies belongs to HIE III (22%).

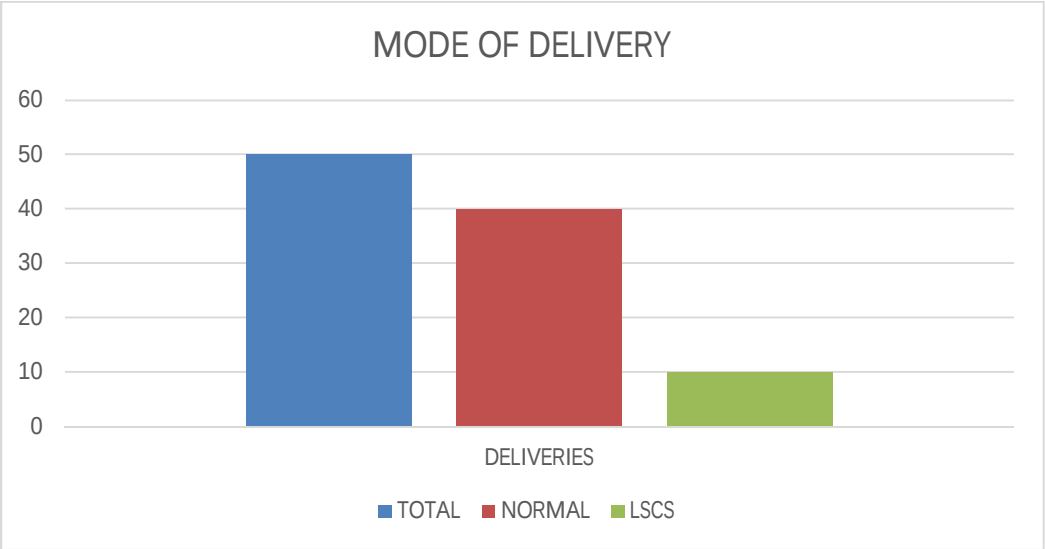
TABLE 10

DESCRIPTIVE ANALYSIS OF MODE OF DELIVERY

NORMAL DELIVERY	LSCS
40	10

FIGURE 15

BAR CHART COMPARING THE MODE OF DELIVERY



In our study out of 50 babies, 40 babies had a normal vaginal delivery (80%) rest 20% had LSCS

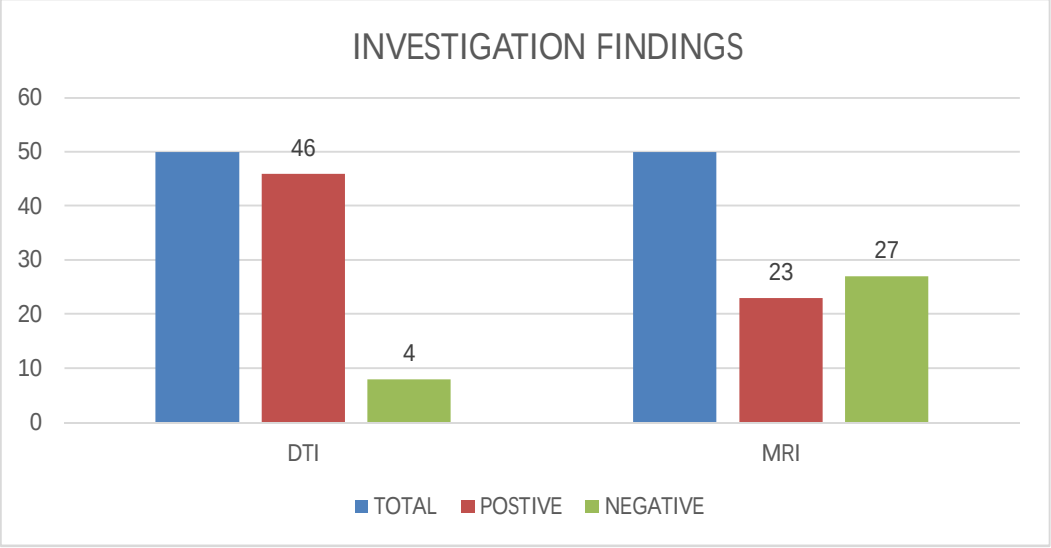
TABLE 11

DESCRIPTIVE ANALYSIS OF DTI & MRI POSITIVE CASES

STUDY	POSTIVE	Percentage	NEGATIVE	Percentage
DTI	46	96%	`4	8%
MRI	23	46%	27	54%

FIGURE 16

BAR CHART COMPARING DTI & MRI POSITIVE CASES



In our study out of 50 babies, DTI picked up abnormalities in 46 babies (92%). But conventional MRI picked out only 23 babies ie 46% alone.

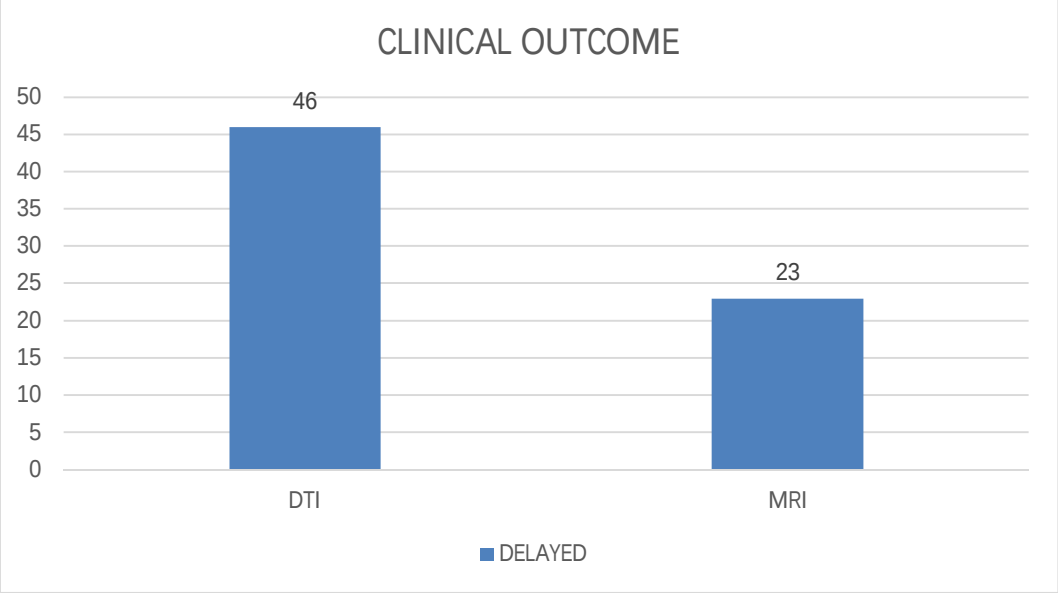
TABLE 12

DESCRIPTIVE ANALYSIS OF POSITIVE CASES AND CLINICAL OUTCOME

INVESTIGATION	POSITIVE CASES	DELAYED CLINICAL OUTCOME
DTI	46/50	42/50
MRI	23/50	42/50

FIGURE 17

BAR CHART SHOWING COMPARISON OF POSITIVE CASES AND CLINICAL OUTCOME



In our study out of 50 babies, picked up by DTI were 42 babies All 42 babies showed delayed development (84%) but in babies picked up by MRI were 23babies out of 50 babies but clinically 42 babies showed delayed development.

TABLE 13

DESCRIPTIVE ANALYSIS OF GESTATIONAL AGE, HIE INJURY & IMAGING MODALITIES.

Gestational age	Total	HIE I	HIE II	HIE III	MRI +ve	DTI +ve
Term	33	17	8	8	18	31
Preterm	17	6	8	3	6	15

TABLE 14

DESCRIPTIVE ANALYSIS OF HIE BABIES WITH POSITIVE CASES

Gestational age	HIE I		HIE II		HIE III	
	DTI +	MRI+	DTI+	MRI+	DTI+	MRI+
TERM	15	6	8	4	8	8
PRETERM	4	1	8	2	3	3
TOTAL	19	7	16	6	11	11

In our study among HIE III babies both DTI and MRI detected all the 11 babies, there is no significant difference between both the modalities among HIE III babies.

But among HIE II babies DTI detected all 16 (100%) cases but MRI detected only 6 cases (37.5%), so it was found that DTI is superior to conventional MRI in detecting cerebral injury in HIE II babies.

But among HIE I babies DTI detected 19 (82%) cases but MRI detected only 7 cases (30%), so it was found that DTI is superior to conventional MRI in detecting cerebral injury in HIE I babies.

DTI failed to detect 4 babies, in follow-up the 4 babies were found to show normal development.

TABLE 15

DESCRIPTIVE ANALYSIS OF POSITIVE FINDINGS WITH CLINICAL OUTCOME

	TOTAL	DTI+VE	BABIES WITH DELAYED DEVELOPMENT
HIE 1	**23**	**19**	**15**
HIE 2	**16**	**16**	**16**
HIE 3	**11**	**11**	**11**
TOTAL	**50**	**46**	**42**

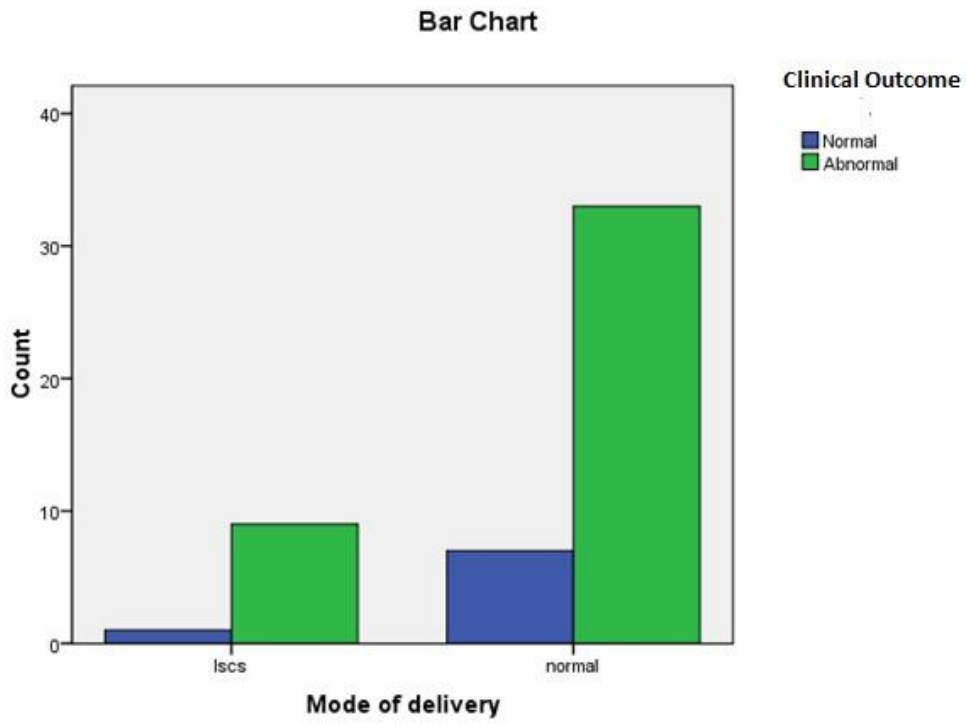
Among 46 babies detected by DTI 42 of them showed delayed development, but 4 babies showed normal development by 1 year of age.

TABLE 16

CORRELATION BETWEEN MODE OF DELIVERY AND CLINICAL OUTCOME

Mode of delivery		outcome		Total	P value
		Normal	Abnormal		
LSCS	count	1	9	10	0.563
	%within mode of delivery	10.0%	90.0%	100.0%	
	% within clinical outcome	12.5%	21.4%	20.0%	
	% of total	2.0%	18.0%	20.0%	
Normal	count	7	33	40	
	%within mode of delivery	17.5%	82.5%	100.0%	
	% within clinical outcome	87.5%	78.6%	80.0%	
	% of total	14.0%	66.0%	80.0%	
Total	Count	8	42	50	
	% within Mode of delivery	16.0%	84.0%	100.0%	
	% within HPE	100.0%	100.0%	100.0%	
	% of Total	16.0%	84.0%	100.0%	

FIGURE 18



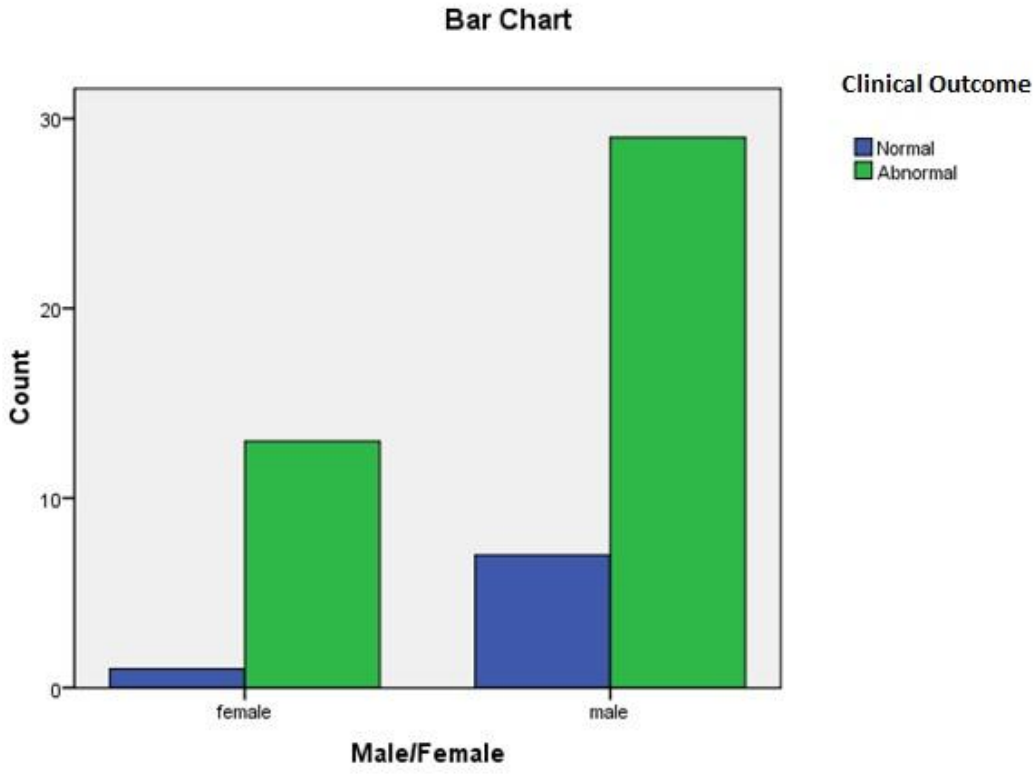
There was no statistical significance between mode of delivery and development of the child.

TABLE: 17

CORRELATION BETWEEN GENDER AND CLINICAL OUTCOME

		Outcome			
female		Normal	Abnormal	Total	P Value
	Count	1	13	14	
	% within Male/Female	7.1%	92.9%	100.0%	
	% within clinical outcome	12.5%	31.0%	28.0%	
male	% of Total	2.0%	26.0%	28.0%	
	Count	7	29	36	
	% within Male/Female	19.4%	80.6%	100.0%	
	% within clinical outcome	87.5%	69.0%	72.0%	0.287
Total	% of Total	14.0%	58.0%	72.0%	
	Count	8	42	50	
	% within Male/Female	16.0%	84.0%	100.0%	
	% within clinical outcome	100.0%	100.0%	100.0%	
	% of Total	16.0%	84.0%	100.0%	

FIGURE 19



Among the 14 female babies 13 babies had delayed development and 1 baby had normal development.

Among the 36 male babies 29 babies had delayed development and 7 babies have delayed development.

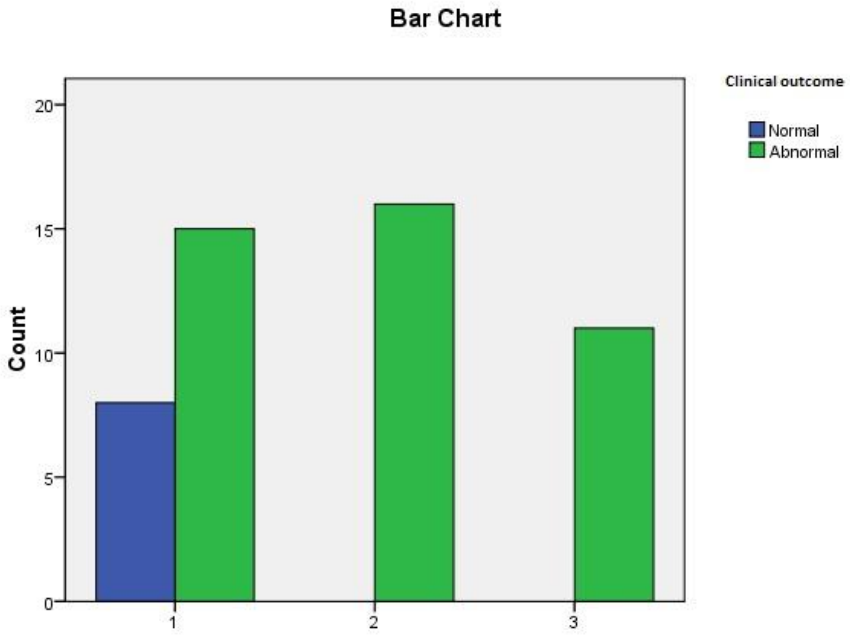
P value is > 0.05 so its not statistically significant.

TABLE 18

CORRELATION BETWEEN MILD, MODERATE & SEVERE HIE (HIE STAGE 1,II,III) AND CLINICAL OUTCOME

		Clinical outcome			
		Normal	Abnormal	Total	P value
HIE I	Count	8	15	23	.004
	% within HIE	34.8%	65.2%	100.0%	
	% within clinical outcome	100.0%	35.7%	46.0%	
	% of Total	16.0%	30.0%	46.0%	
2	Count	0	16	16	
	% within HIE	.0%	100.0%	100.0%	
	% within clinical outcome	.0%	38.1%	32.0%	
	% of Total	.0%	32.0%	32.0%	
3	Count	0	11	11	
	% within HIE	.0%	100.0%	100.0%	
	% within clinical outcome	.0%	26.2%	22.0%	
	% of Total	.0%	22.0%	22.0%	
Total	Count	8	42	50	
	% withinHIE	16.0%	84.0%	100.0%	
	% within clinical outcome	100.0%	100.0%	100.0%	
	% of Total	16.0%	84.0%	100.0%	

FIGURE 20



Among the 23 HIE I babies 15 babies had delayed development and 8 babies had normal development.

Among the 16 HIE 2 babies all the 16 babies had delayed development.

Among the 11 HIE III babies all the 11 babies had delayed development

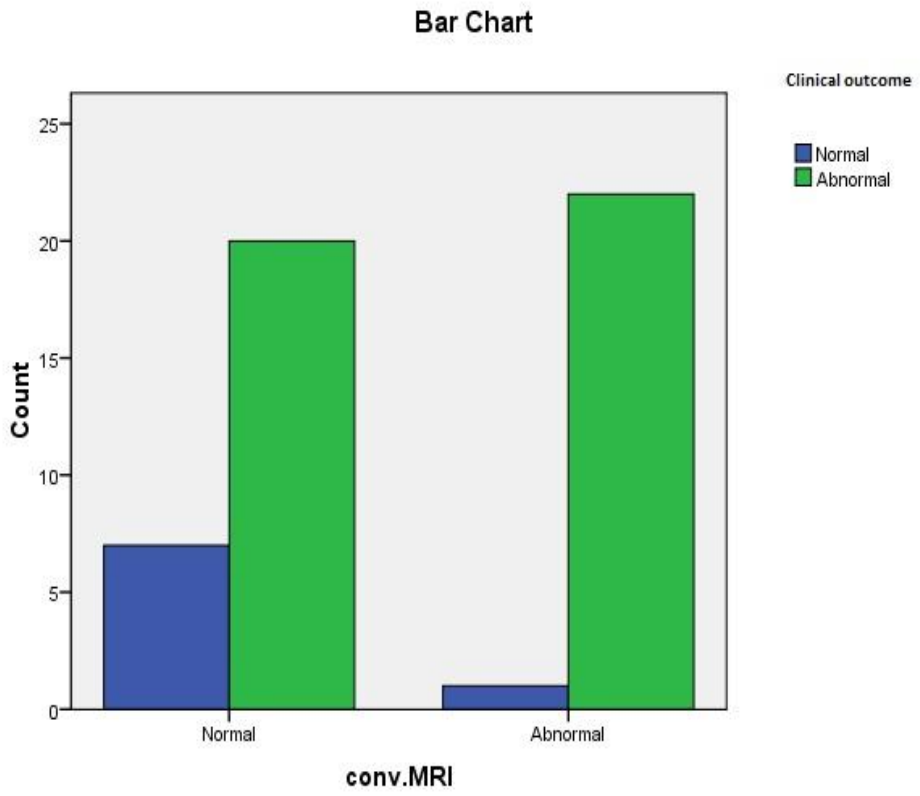
P value 0.004 its statistically significant.

TABLE 19

CORRELATION BETWEEN CONVENTIONAL MRI FINDINGS WITH CLINICAL OUT COME

		Clinical outcome				
			normal	abormal	TOTAL	P VALUE
conv.MRI	Normal	Count	7	20	Total 27	.001
	% within HIE	% within conv.MRI	25.9%	74.1%		
	% within clinical outcome	% within outcome	87.5%	47.6%	100.0%	
	% of Total	% of Total	14.0%	40.0%	54.0%	
	Abnormal	Count	1	22	54.0% 23	
	% within HIE	% within conv.MRI	4.3%	95.7%		
	% within clinical outcome	% within outcome	12.5%	52.4%	100.0%	
	% of Total	% of Total	2.0%	44.0%	46.0%	
	Total	Count	8	42	46.0% 50	
	% within HIE	% within conv.MRI	16.0%	84.0%		
	% within clinical outcome	% within outcome	100.0%	100.0%	100.0%	
	% of Total	% of Total	16.0%	84.0%		

FIGURE 21



Among the 50 babies conventional MRI detected 27 babies with abnormal findings, with in the 27 babies 20 babies had delayed development and 7 babies had normal development.

Conventional MRI failed to detect 23 babies, among them 22 babies had delayed development and 1 baby had normal development.

Conventional MRI failed to detect 22 babies with delayed development.

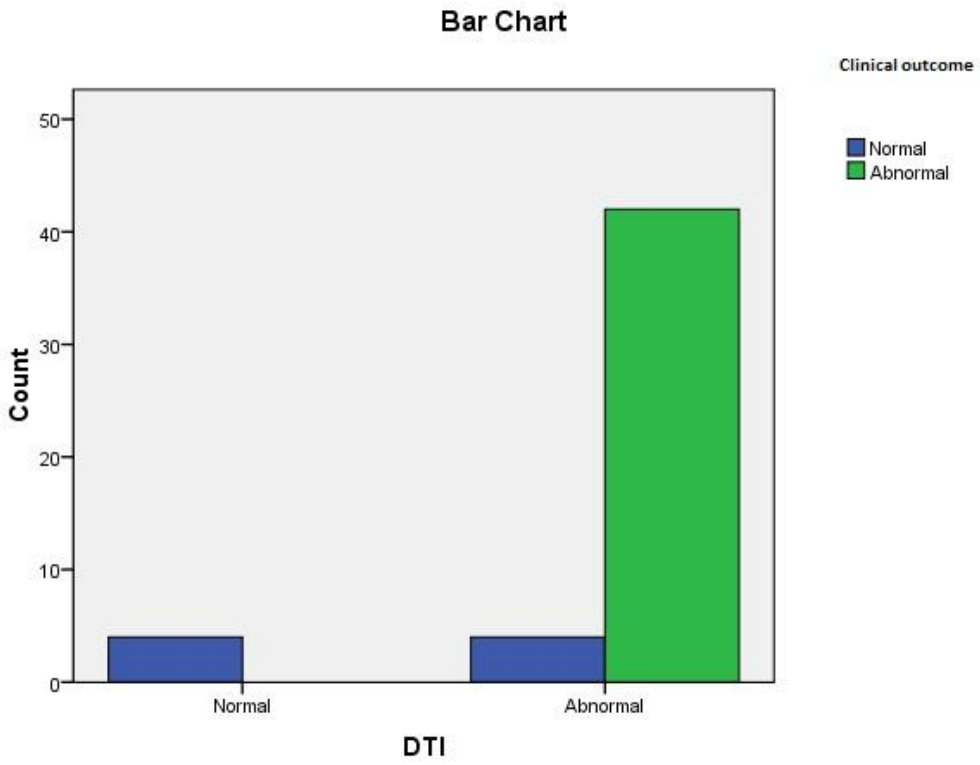
P value is <0.005 so its statistically significant.

TABLE 20

CORRELATION BETWEEN DTI FINDINGS WITH CLINICAL OUT COMES

		Clinical outcome			
DTI		Normal	Abnormal	Total	P value
Normal	Count	4	0	4	
	% within DTI	100.0%	.0%	100.0%	
	% within clinical outcome	50.0%	.0%	8.0%	
	% of Total	8.0%	.0%	8.0%	
Abnormal	Count	4	42	46	
	% within DTI	8.7%	91.3%	100.0%	0.0125
	% within clinical outcome	50.0%	100.0%	92.0%	
	% of Total	8.0%	84.0%	92.0%	
Total	Count	8	42	50	
	% within DTI	16.0%	84.0%	100.0%	
	% within clinical outcome	100.0%	100.0%	100.0%	
	% of Total	16.0%	84.0%	100.0%	

FIGURE 22



Among the 50 babies DTI detected 46 babies among them 42 showed delayed development and 4 babies had normal development.

P value <0.05 so its statistically significant.

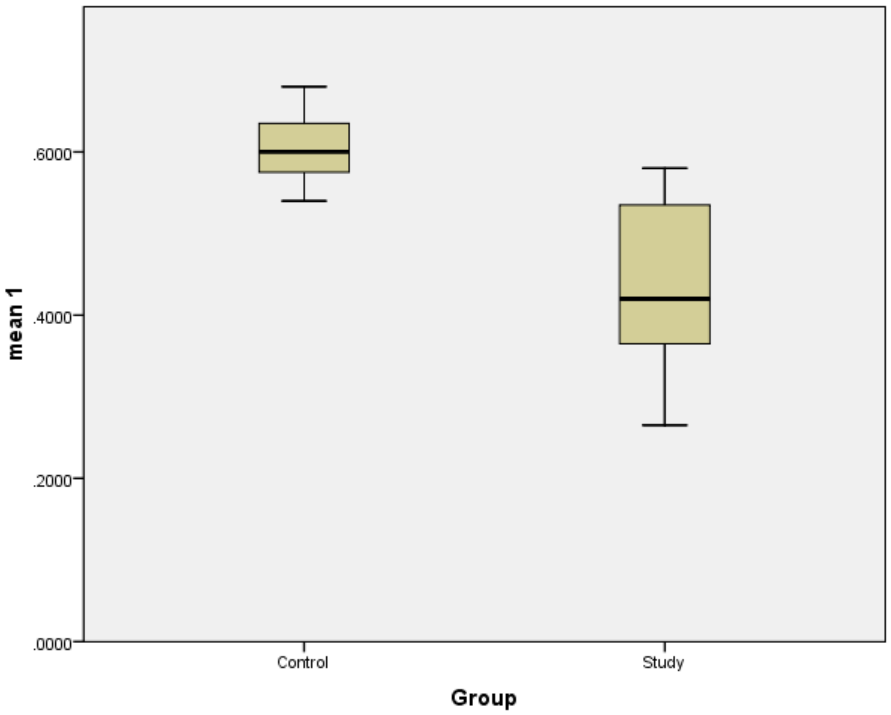
TABLE 21

COMPARING FA VALUE IN CORONA RADIATA IN STUDY AND CONTROL GROUP

Group Statistics

	Corona Radiata	N	Mean	Std. Deviation	Std. Error Mean	P
mean 1	Control	20	.600500	.0416091	.0093041	0.000 SIGNIFICANT
	Study	50	.439500	.1046922	.0148057	

FIGURE 23



On comparing the mean FA value of control and study group the P value is 0.00 it is statistically significant.

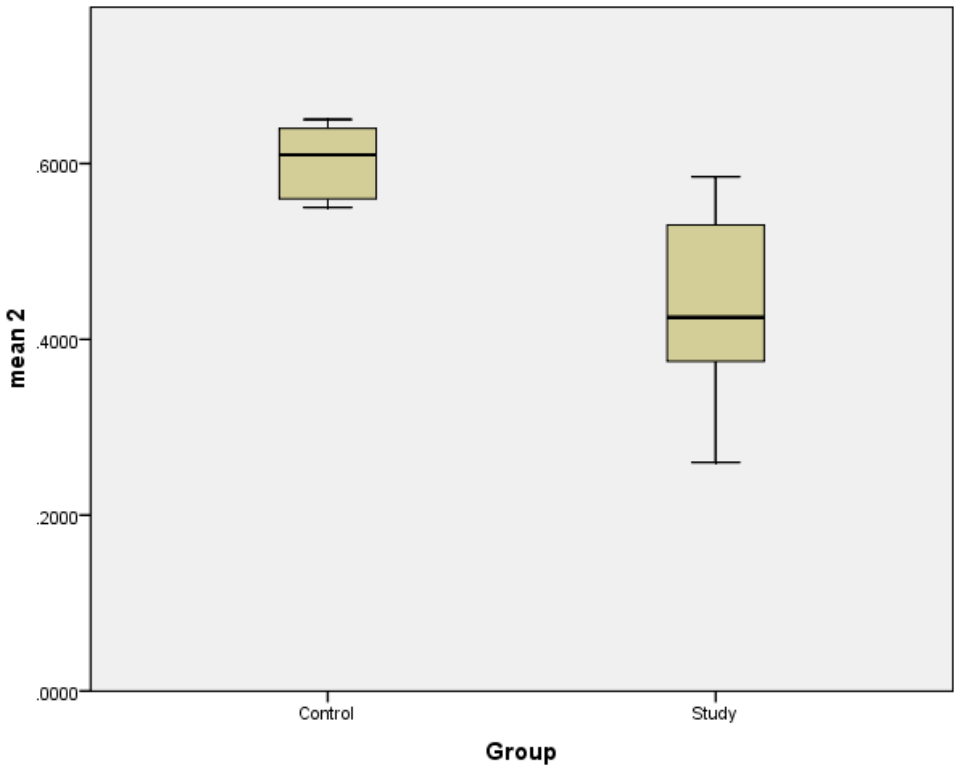
TABLE 22

COMPARING FA VALUE IN ANTERIOR LIMB OF INTERNAL CAPSULE IN STUDY AND CONTROL GROUP

Group Statistics

	Anterior Limb of IC	N	Mean	Std. Deviation	Std. Error Mean	P
mean 2	Control	20	.601000	.0391891	.0087630	0.000 SIGNIFICANT
	Study	50	.439830	.0946094	.0133798	

FIGURE 24



On comparing the mean FA value of control and study group the P value is 0.00 it is statistically significant.

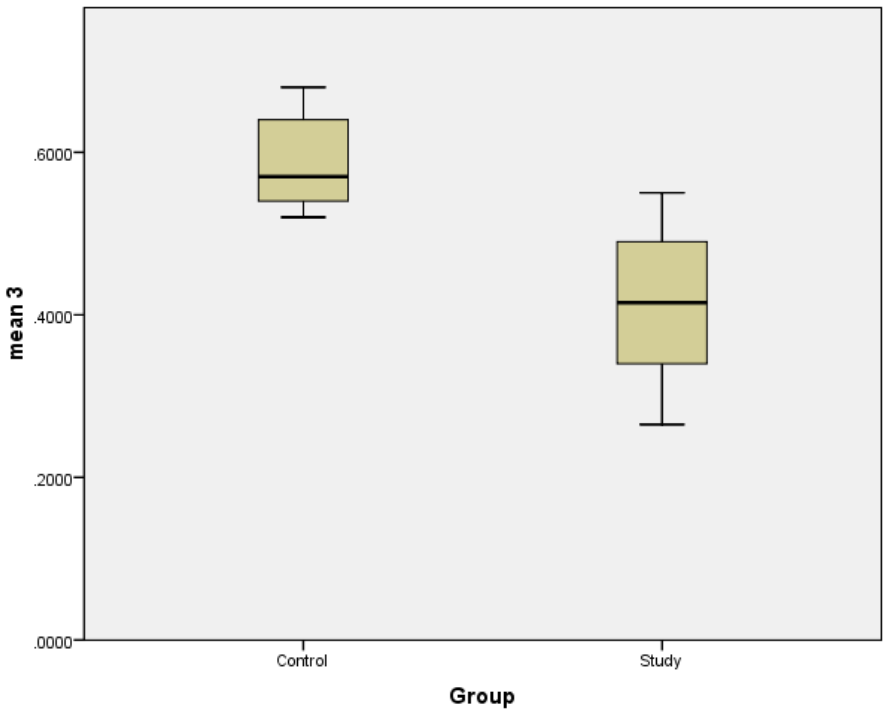
TABLE 23

COMPARING FA VALUE IN POSTERIOR LIMB OF INTERNAL CAPSULE IN STUDY AND CONTROL GROUP

Group Statistics

	Posterior Limb of IC	N	Mean	Std. Deviation	Std. Error Mean	P
mean 3	Control	20	.594000	.0626099	.0140000	0.000 SIGNIFICANT
	Study	50	.421100	.0810788	.0114663	

FIGURE 25



On comparing the mean FA value of control and study group the P value is 0.00 it is statistically significant.

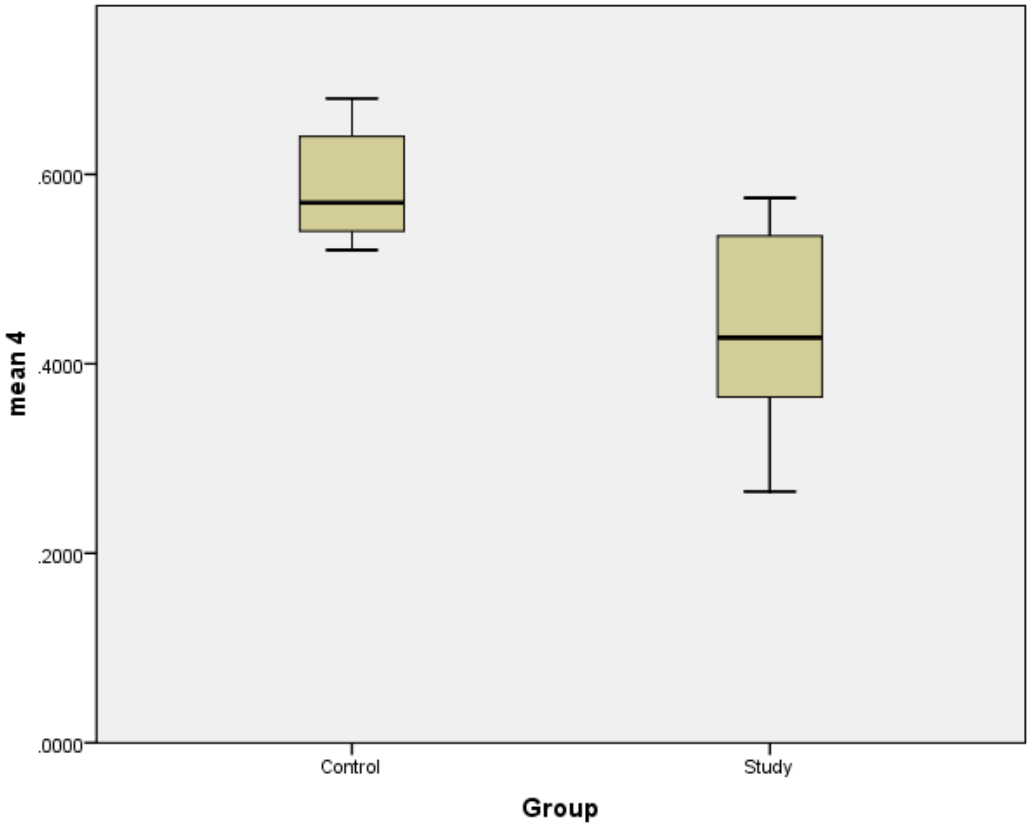
TABLE 24

COMPARING FA VALUE IN SLF IN STUDY AND CONTROL GROUP

Group Statistics

	SLF	N	Mean	Std. Deviation	Std. Error Mean	P
mean 4	Control	20	.594000	.0626099	.0140000	0.000 SIGNIFICANT
	Study	50	.442730	.0937615	.0132599	

FIGURE 26



On comparing the mean FA value of control and study group the P value is 0.00 it is statistically significant.

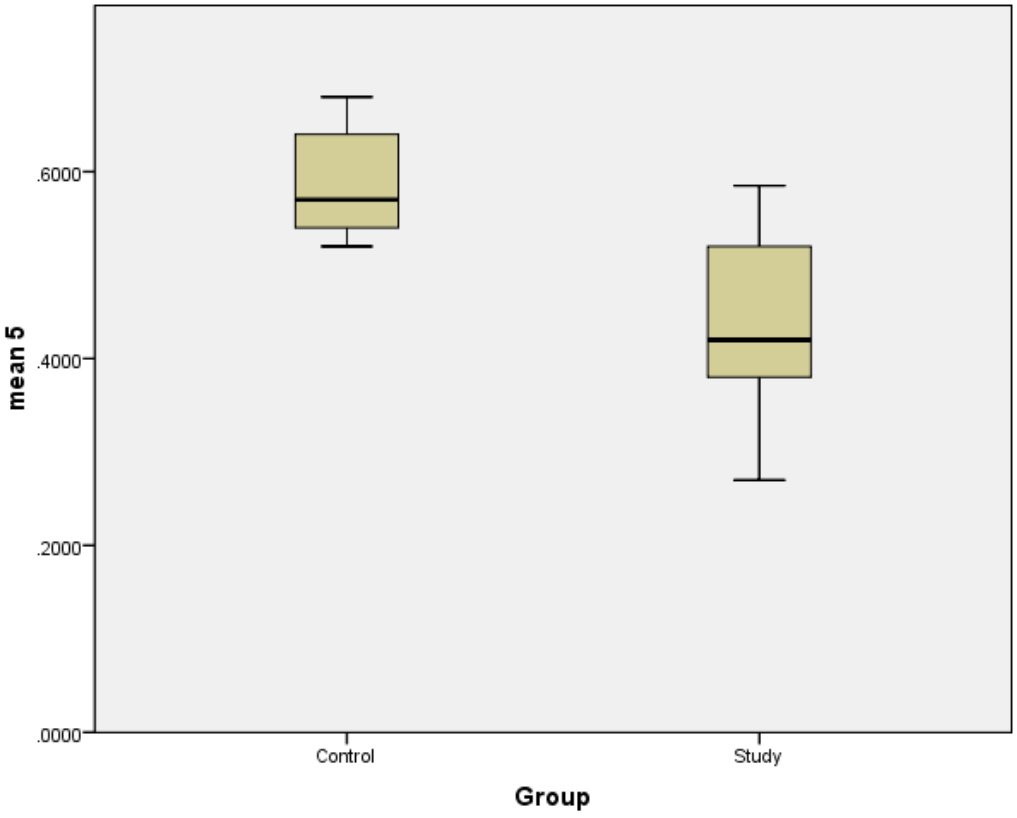
TABLE 25

COMPARING FA VALUE IN ILF IN STUDY AND CONTROL GROUP

Group Statistics

	ILF	N	Mean	Std. Deviation	Std. Error Mean	P
mean 5	Control	20	.594000	.0626099	.0140000	0.000 SIGNIFICANT
	Study	50	.433700	.0942955	.0133354	

FIGURE 27



On comparing the mean FA value of control and study group the P value is 0.00 it is statistically significant.

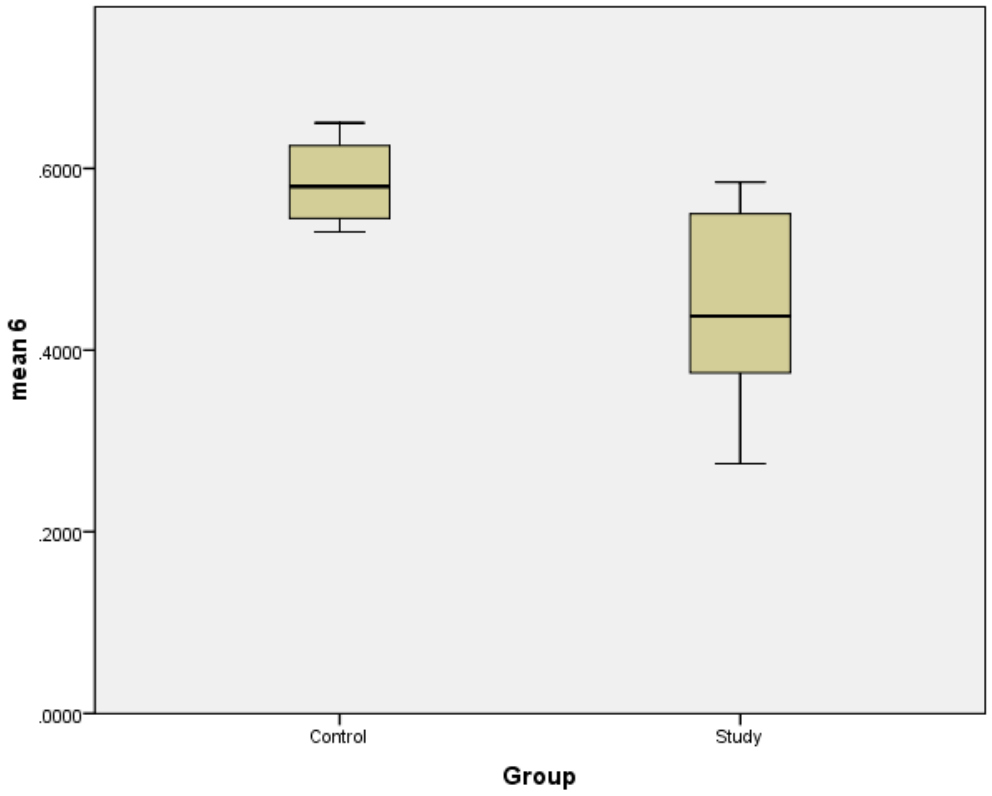
TABLE 26

COMPARING FA VALUE IN CINGULATE GYRUS IN STUDY AND CONTROL GROUP

Group Statistics

	Cingulate gyrus	N	Mean	Std. Deviation	Std. Error Mean	P
mean 6	Control	20	.582000	.0452595	.0101203	0.000 SIGNIFICANT
	Study	48	.447917	.1005931	.0145194	

FIGURE 28



On comparing the mean FA value of control and study group the P value is 0.00 it is statistically significant.

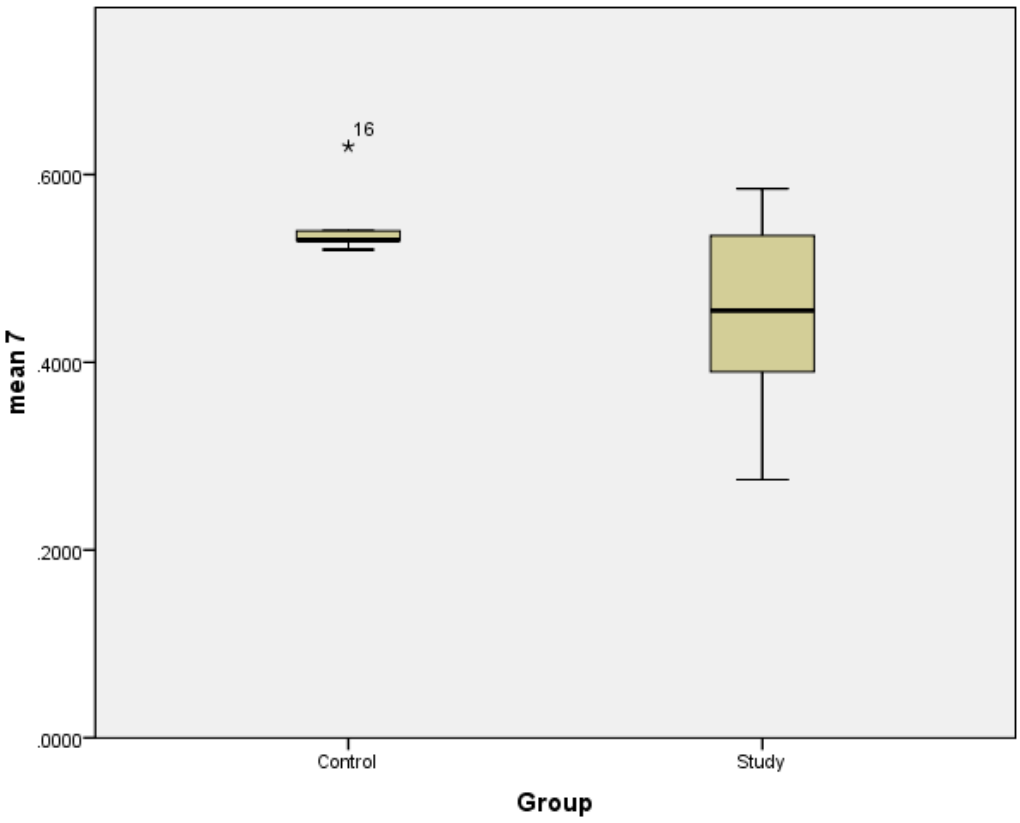
TABLE 27

COMPARING FA VALUE IN THALAMUS IN STUDY AND CONTROL GROUP

Group Statistics

	Thalamus	N	Mean	Std. Deviation	Std. Error Mean	P
mean 7	Control	20	.536000	.0232605	.0052012	0.000 SIGNIFICANT
	Study	50	.444000	.0947661	.0134019	

FIGURE 29



On comparing the mean FA value of control and study group the P value is 0.00 it is statistically significant.

TABLE 21

SCREENING TEST EVALUATION

	MRI	DTI
Sensitivity	52.38%	100%
Specificity	87.5%	90%
Positive Predictive Value	95.65%	91.3%
Negative Predictive Value	25.93%	96%
Diagnostic Accuracy	58%	92%

DISCUSSION

In our study there were no significant differences in ADC values among the different stages of HIE , which was consistent with a previous study done by **van Laerhoven et al.,** 2013.[{62}]

In our study, in 5 babies MRI imaging was done within 7 days of life. All the 5 babies showed abnormality in ADC value and also had diffusion restriction. Which was consistent with study done by **Winter et al., 2007**[{63}.]

Who says that ADC values are more useful in the early diagnosis of HIE, and pseudo-normalization of ADC values occur after the acute stageand another study done by **Guo et al. 2016**[{64}] reported that within seven days after birth, DWI used to detect ADC values showed that the HIE sensitivity was 83%, specificity was 63% and positive predictive value was 83%.

In our study only 5 babies were underwent imaging within 5 days of life. Rest of the 45 babies were imaged after 7 days of life, because of unstable vitals and most of the babies were desaturated without oxygen support. This is agreed with study done by **Li et al., 2014** **{65}** says that in the acute stage possibly the babies had severe lesions and unstable vital signs in each group. MRI examination was difficult in the acute phase.

In our study 45 babies were screened after 7 days so life so they had no significant abnormality in diffusion weighted imaging and ADC values .It is consistent with study done by de **Vries et al, 2011**.{66} have revealed that the diagnostic value of ADC values in the subacute stage is decreased

Our study results demonstrated that the FA values had a high diagnostic value. and FA values were markedly decreased in the dense white matter, splenium of the corpus callosum, and posterior limbs of the internal capsules. Decreased FA values are related to cell death and loss of structural components of white matter fibers.as says by **Rutherford et al**. 1998{67} demonstrated that apoptosis was more obvious than necrosis in children in the subacute stage of HIE, this could explain why FA values decreased, but ADC values were normal.

In this study, MRI in 6 cases of moderate HIE children revealed symmetric high-signal intensity in the thalami, but FA values were reduced in the thalami. This type of basal ganglia/thalamus injury can cause athetoid cerebral palsy as says by **de Vries et al., 2011**(65). and shows the possibility of severe cognitive impairment as says by Li et al., 2016(66).

In our study 50 babies were selected with APGAR score of less than 7. All babies were investigated by MRI within 14 days of life. In our study out of 50 babies 33 term babies and 17 preterm babies were included. Among these babies 17 babies were under 2.5 kg birth weight and 33 babies were more than 2.5kg.Among them 40 babies were delivered by normal vaginal delivery and 10 had LSCS. There was no statistical difference in gravidity, parity, gestation, birth weight, sex, mode of delivery,

In our study 23 babies came under HIE -1, 16 babies were under HIE II and 11 babies were under HIE III. Among HIE 1 babies conventional MRI picked up 7 (30%) babies with abnormal ADC values in posterior limb of internal capsule rest of the 17 babies didn't show any finding. In DTI all 23 babies showed abnormal FA value in posterior limb of internal capsule.

Among the 16 babies in HIE 2, conventional MRI picked up 6 (37.5%) babies with HIE II and shows diffusion restriction in anterior and posterior limb of internal capsule, splenium of corpus callosum, peritrigonal white matter areas.DTI picked up all 16 babies (100%) and shows abnormal FA value in anterior and posterior limb of internal capsule, splenium of corpus callosum, peritrigonal white matter areas ,superior & inferior longitudinal fasciculus and cingulate gyrus.

Among 11 babies with HIE III, conventional MRI picked out all 11 babies (100%) and shows diffusion restriction in anterior and posterior limb of internal capsule, splenium of corpus callosum, peritrigonal white matter areas, basal ganglia and thalamus.DTI also picked up 11 babies (100%) and showed abnormal FA value in anterior and posterior limb of internal capsule, splenium of corpus callosum, peritrigonal white matter areas, basal ganglia and thalamus.

In our study DTI of HIE babies shows abnormal FA values in the affected regions. Normal FA values ranges from 0.5 – 1.0. In our study HIE I babies shows FA value ranges between 0.5+/-0.007. HIE II shows FA values 0.4+/-0.01 & HIE III shows FA values of 0.3 +/- 0.03.Pre term babies showed less severe involvement of basal ganglia and term babies shows frequent involvement of peri rolandic cortex.

Periventricular leukomalacia is associated with mild to moderate asphyxia in preterm neonates. In a study conducted by **ZHANG *et al*,** supported our study demonstrated that DTI provides sensitive detection and early diagnosis of WM injuries in premature infants with HIE.In our study out of 17 preterm babies with HIE, DTI detected 15 babies. [68]

In moderate asphyxia posterior limb of internal capsule , posterolateral lentiform nucleus and lateral thalamus are more commonly involved.

HIE III babies shows abnormality in posterior limb of internal capsule , basal ganglia, thalamus, cerebral cortex.

All the 50 babies were followed up for 1 year and their clinical milestones were examined at 4 months interval with Denver developmental scale.

42/46 (91.3%) babies picked out by DTI showed developmental delay at the endplate of 1 year. But MRI was only able to pickup 23 babies out of 42 babies (54%) who showed developmental delay.

FA values in ROIs quantitatively assess the white matter injury in neonates with HIE. The changes in FA value is most obvious in the posterior limbs of the internal capsules, and shows accurate and objective assessment of the degree of white matter injury in babies with HIE.

DTI has important clinical significance, and can accurately and objectively assess the prognosis of babies with HIE .Limitation of this study was there were less number of cases included in this study and unqual number of cases in term and pre term babies.FA value was calculated in randomly selected 7 areas in brain. Control babies we were selected were not normal babies ,they were referred for MRI brain for other than HIE.

CONCLUSION

From our study we came to find out that HIE -1 mainly affects the posterior limb of internal capsule and HIE III diffusely affects the white matter ,basal ganglia and thalamus.

In summary, DTI is currently the only way to quantify the maturation and damage of brain development in preterm neonates. In the early stage, it can identify damages that cannot be screened by MRI. Thus, it can provide evidence for developing effective measures of prevention, protection, and rehabilitation for damage to the brain. Coupled with a good intervention. treatment system established with clinical development assessment and pathogenic factors, DTI is an important aid to improve the prognosis of nerve development for preterm neonates, owing to its ability to reflect the damage to cells in white matter and nerve fibers at an early stage and at a microscopic level.

In our study, both the sensitivity and specificity are high for DTI compared to conventional MRI.

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ABBREVIATIONS

DTI	-	Diffusion Tensor Imaging
MRI	-	magnetic Resonance Imaging
STIR	-	Short Tau Inversion Recovery
FSE	-	Fast spin Echo
NO	-	Nitric Oxide
NOS	-	nitric Oxide Synthase
NMDA	-	N-methyl-D-aspartate receptor
AMPA	-	α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor
VDCC	-	Voltage Dependent Calcium Channel
HIE	-	Hypoxic Ishcemic Encephalopathy
FSE-IR	-	Fast spin echo Inversion recovery
PVHI	-	Periventricular hemorrhagic infract
FT	-	Fiber Tractography
FA	-	Fractional Anisotrophy
MD	-	Mean Diffusivity
ADC	-	Apparent Diffusion Coefficent
ECMO	-	Extra Corporeal Membrane Oxygenation
DDST	-	Denever Developmental Screening Test.

PROFORMA

- NAME:
- AGE:
- DATE OF BIRTH:
- ADDRESS:
- MOBILE NUMBER:
- PARENTS NAME:
- GESTATIONAL AGE:
- BIRTH WEIGHT:
- APGAR SCORE AT I AND 5 MIN:
- HIE STAGE:
- FINDINGS IN CONVENTIONAL MRI IMAGING:
- FINDINGS IN DIFFUSION TENSOR IMAGING:
- CLINICAL ASSESSMENT DURING SERIAL FOLLOW UP:

PATIENT CONSENT FORM

Study detail :

PROSPECTIVE STUDY OF DIFFUSION TENSOR IMAGING AND CONVENTIONAL MAGNETIC RESONANCE IMAGING IN TERM AND PRETERM NEONATES WITH HYPOXIC ISCHEMIC ENCEPHALOPHY AND CORRELATION WITH CLINICAL OUTCOME

Study Centre : Govt. Kilpauk Medical College

Hospital, Chennai

Patients Name :

Patients Age :

Identification Number :

Patient may check ( ) these boxes

I confirm that I have understood the purpose of procedure for the above study. I had the opportunity to ask question and all my questions and doubts have been answered to my complete satisfaction.

I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving reason, without my legal rights being affected.

I understand that sponsor of the clinical study, others working on the sponsor's behalf, the ethical committee and the regulatory authorities will not need my permission to look at my health records, both in respect of current study and any further research that may be conducted in relation to it, even if I withdraw from the study I agree to this access. However, I understand that my identify will not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from this study.

I hereby make known that I have fully understood the use of above procedure, the possible complications arising out of its use and the same was clearly explained to me.

I agree to take part in the above study and to comply with the instruction given during the study and faithfully cooperate with the study team and to immediately inform the study staff if I suffer from any deterioration in my health or well-being or any unexpected or unusual symptoms.

I hereby consent to participate in this study.

I hereby give permission to undergo complete clinical examination and diagnostic tests including hematological, biochemical, radiological tests.

Signature / thumb impression :

Patients Name and Address: Place Date

Signature of Investigator :

Study Investigator's Name : Place Date

PATIENT INFORMATION LEAFLET

PROSPECTIVE STUDY OF DIFFUSION TENSOR IMAGING AND CONVENTIONAL MAGNETIC RESONANCE IMAGING IN TERMAND PRETERM NEONATES WITH HYPOXIC ISCHEMIC ENCEPHALOPHY AND CORRELATION WITH CLINICALOUTCOME

Study place –, Government Kilpauk Medical College Hospital, Chennai.

We wish you to take part in a research study.

- Before you decide whether to take part, it is important for you to understand why research is being done and what it will involve.
- Please take time to read the following information carefully. Discuss it with friends and relatives. Take time to decide whether you want to participate in the study or not.
- You are free to decide whether or not to take part in this research study. If you choose not to participate, this will not affect the care you get from your doctors.
- Ask us if there is anything that is not clear or if you want more information.
- Thank you for reading this information. If you decide to take part you will be given a copy of this information sheet and your signed consent form.

Signature of the investigator Signature of the participant

Date:

நோயாளி ஒப்புதல் படிவம்

ஆராய்ச்சியின் விவரம்:

ஆராய்ச்சி மையம்:

நோயாளியின் பெயர்: நோயாளியின் வயது:

பதிவு எண்:

நோயாளி கீழ்கண்டவற்றுள் கட்டங்களை (✓) செய்யவும்

1. மேற்குறிப்பிட்டுள்ள ஆராய்ச்சியின் நோக்கத்தையும் பயனையும் முழுவதுமாக புரிந்துகொண்டேன். மேலும் எனது அனைத்து சந்தேகங்களையும் கேட்டு அதற்கான விளக்கங்களையும் தெளிவுபடுத்திக் கொண்டேன். ☐

2. மேலும் இந்த ஆராய்ச்சிக்கு எனது சொந்த விருப்பத்தின் பேரில் பங்கேற்கிறேன் என்றும், மேலும் எந்த நேரத்திலும் எவ்வித முன்னறிவிப்புமின்றி இந்த ஆராய்ச்சியிலிருந்து விலக முழுமையான உரிமை உள்ளதையும், இதற்கு எவ்வித சட்ட பிணைப்பும் இல்லை என்பதையும் அறிவேன். ☐

3. ஆராய்ச்சியாளரோ, ஆராய்ச்சி உதவியாளரோ, ஆராய்ச்சி உபயத்தாரோ, ஆராய்ச்சி பேராசிரியரோ, ஒழுங்குநெறி செயற்குழு உறுப்பினர்களோ எப்போது வேண்டுமானாலும் எனது அனுமதியின்றி எனது உள்நோயாளி பதிவுகளை இந்த ஆராய்ச்சிக்காகவோ அல்லது எதிர்கால பிற ஆராய்ச்சிகளுக்காகவோ பயன்படுத்திக்கொள்ளலாம் என்றும், மேலும் இந்த நிபந்தனை நான் இவ்வாராய்ச்சியிலிருந்து விலகினாலும் தரும் என்றும் ஒப்புக்கொள்கிறேன். ஆயினும் எனது அடையாளம் சம்பந்தப்பட்ட எந்த பதிவுகளும் சட்டபூர்வமான தேவைகள் தவிர வெளியிடப்படமாட்டாது என்ற உறுதிமொழியின் பெயரில் இந்த ஆராய்ச்சியிலிருந்து கிடைக்கப்பெறும் முடிவுகளை வெளியிட மறுப்பு தெரிவிக்கமாட்டேன் என்று உறுதியளிக்கின்றேன். ☐

4. இந்த ஆராய்ச்சிக்கு நான் முழுமனதுடன் சம்மதிக்கின்றேன் என்றும் மேலும் ஆராய்ச்சிக் குழுவினர் எனக்கு அளிக்கும் அறிவுரைகளை தவறாது பின்பற்றுவேன் என்றும் இந்த ஆராய்ச்சி காலம் முழுவதும் எனது உடல் நிலையில் ஏதேனும் மாற்றமோ அல்லது எதிர்பாராத பாதகமான விளைவோ எற்படுமாயின் உடனடியாக ஆராய்ச்சி குழுவினரை அணுகுவேன் என்றும் உறுதியளிக்கின்றேன். ☐

5. இந்த ஆராய்ச்சிக்குத் தேவைப்படும் அனைத்து மருத்துவப் பரிசோதனைகளுக்கும் ஒத்துழைப்பு தருவேன் என்று உறுதியளிக்கின்றேன். ☐

6. இந்த ஆராய்ச்சிக்கு யாருடைய வற்புறுத்தலுமின்றி எனது சொந்த விருப்பத்தின் பேரிலும் சுயஅறிவுடனும் முழுமனதுடனும் சம்மதிக்கின்றேன் என்று இதன் மூலம் ஒப்புக்கொள்கிறேன். ☐

நோயாளியின் கையொப்பம் / பெருவிரல் கைரேகை ஆராய்ச்சியாளரின் கையொப்பம்

இடம்: தேதி:

Sl.NO	NAME	rth weight g	ode of delive	Male/Female	APGAR scor	LIFE on inv	TERM	1 DTI right	1 DTI left	2 DTI right	2 DTI left	DTI right	DTI left	DTI right	DTI left	DTI right	DTI left	DTI right	DTI left	DTI right	DTI left
1	B/O rudra	2850.00	lscs	female	6.00	10.00	Term	0.57	0.58	0.60	0.58	0.52	0.54	0.55	0.56	0.58	0.63	0.68	0.59	0.58	0.53
2	B/O kalaiselv	2550.00	normal	male	4.00	13.00	Pre term	0.60	0.56	0.56	0.68	0.64	0.64	0.68	0.64	0.68	0.62	0.57	0.52	0.57	0.54
3	B/O selvi	2900.00	normal	female	5.00	13.00	PRETERM	0.64	0.56	0.66	0.65	0.68	0.69	0.58	0.57	0.55	0.57	0.51	0.53	0.57	0.55
4	B/O ayisha	1240.00	normal	male	5.00	9.00	PRETERM	0.62	0.63	0.60	0.67	0.54	0.57	0.58	0.57	0.54	0.53	0.54	0.52	0.57	0.59
5	B/O ashwin	2650.00	normal	female	4.00	8.00	TERM	0.68	0.64	0.57	0.54	0.53	0.51	0.52	0.58	0.57	0.59	0.52	0.54	0.51	0.58
6	B/O sangeeth	2870.00	normal	female	4.00	11.00	TERM	0.65	0.66	0.63	0.68	0.54	0.57	0.58	0.57	0.54	0.53	0.54	0.52	0.57	0.59
7	B/o devi	2850.00	lscs	male	5.00	12.00	Term	0.54	0.55	0.59	0.54	0.54	0.57	0.58	0.57	0.54	0.53	0.54	0.52	0.57	0.59
8	B/O aarthi	3100.00	normal	female	5.00	5.00	Term	0.68	0.64	0.57	0.54	0.53	0.51	0.52	0.58	0.57	0.59	0.52	0.54	0.51	0.58
9	B/o ramya	1750.00	normal	male	6.00	10.00	Preterm	0.60	0.58	0.56	0.68	0.64	0.64	0.68	0.64	0.68	0.62	0.57	0.52	0.57	0.54
10	b mahalaksh	2900.00	normal	male	4.00	10.00	term	0.64	0.56	0.66	0.65	0.68	0.69	0.58	0.57	0.55	0.57	0.51	0.53	0.57	0.55
11	b/o Ashmitha	1900.00	normal	male	6.00	8.00	Preterm	0.59	0.56	0.56	0.68	0.64	0.64	0.68	0.64	0.68	0.62	0.57	0.52	0.57	0.54
12	B/O priya	2580.00	lscs	male	5.00	12.00	term	0.54	0.55	0.59	0.54	0.54	0.57	0.58	0.57	0.54	0.53	0.54	0.52	0.57	0.59
13	B/o Alamelu	2650.00	normal	female	5.00	10.00	Term	0.60	0.56	0.56	0.68	0.64	0.64	0.68	0.64	0.68	0.62	0.57	0.52	0.57	0.54
14	b/o poornima	2000.00	normal	male	4.00	11.00	Term	0.64	0.56	0.66	0.65	0.68	0.69	0.58	0.57	0.55	0.57	0.51	0.53	0.57	0.55
15	B/O janani	2140.00	normal	male	5.00	10.00	preterm	0.67	0.64	0.59	0.56	0.54	0.53	0.52	0.58	0.57	0.59	0.52	0.54	0.51	0.58
16	B/o aishwary	1990.00	normal	male	6.00	11.00	Preterm	0.68	0.64	0.57	0.54	0.53	0.51	0.52	0.58	0.57	0.59	0.52	0.54	0.51	0.58
17	b/o karthika	1890.00	normal	male	6.00	9.00	Preterm	0.57	0.58	0.60	0.58	0.52	0.54	0.55	0.56	0.58	0.63	0.68	0.59	0.58	0.53
18	B/O Sonia	2050.00	normal	male	4.00	7.00	preterm	0.54	0.55	0.59	0.54	0.54	0.57	0.58	0.57	0.54	0.53	0.54	0.52	0.57	0.59
19	B/o suja	2700.00	normal	female	5.00	11.00	Preterm	0.64	0.56	0.66	0.65	0.68	0.69	0.58	0.57	0.55	0.57	0.51	0.53	0.57	0.55
20	B/O Shalini	2900.00	normal	male	6.00	8.00	Term	0.60	0.56	0.56	0.68	0.64	0.64	0.68	0.64	0.68	0.62	0.57	0.52	0.57	0.54

Sl.NO	NAME	Birth weight gms	Mode of delivery	Male/Female	APGAR score	DAY OF LIFE	TERM	HIE	coro0 radiata			anterior limb of Inter0l capsule			posterior limb of Inter0l capsule			SLF			IFOF			cingulate gyrus			thalamus			developmental delay	
									conv.MRI	DTI		conv.MRI	DTI (FA value)		conv.MRI	DTI (FA value)		conv.MRI	DTI (FA value)		conv.MRI	DTI (FA value)		conv.MRI	DTI (FA value)		conv.MRI	DTI (FA value)		yes	no
							/PRETERM	STAGE		Right	Left		Right	Left		Right	Left		Right	Left		Right	Left		Right	Left		Right	Left		
1	B/O VIDYA	2900	normal	male	4	11	Term	3	1	0.29	0.39		0.38	0.28	1	0.51	0.54	1	0.24	0.33	1	0.29	0.32	0	0.25	0.36	0	0.28	0.38	1	
2	B/O Sonia	3100	lscs	male	7	10	Term	1	0	0.4	0.51	0	0.52	0.44	0	0.46	0.51	0	0.58	0.4	0	0.56	0.49	0	0.43	0.55	0	0.54	0.53		0
3	B/O Firoz	2350	normal	male	6	10	Preterm	1	0	0.52	0.45	0	0.46	0.57	0	0.58	0.47	0	0.55	0.46	0	0.57	0.49	0	0.44	0.58	0	0.58	0.59		0
4	B/O shanmughapriya	2750	lscs	male	4	14	Term	3	1	0.37	0.28	1	0.41	0.28	1	0.44	0.24	1	0.22	0.35	1	0.26	0.33	0	0.27	0.33	0	0.25	0.38	1	
5	B/Odhanalakshmi	2870	normal	male	6	13	Term	1	0	0.59	0.56	0	0.46	0.57	0	0.51	0.48	0	0.41	0.56	0	0.23	0.59	0	0.26	0.45	0	0.55	0.54		0
6	B/O jaya	2980	normal	female	7	5	Term	1	0	0.56	0.41	0	0.51	0.47	0	0.56	0.44	0	0.52	0.44	0	0.41	0.53	0	0.52	0.42	0	0.52	0.51		0
7	B/O revathi	2780	lscs	male	7	11	Term	1	0	0.48	0.58	0	0.61	0.46	0	0.49	0.47	0	0.42	0.55	0	0.51	0.49	0	0.57	0.47	0	0.55	0.56		0
8	B/O dhanalkashmi	2150	normal	male	4	10	Pre term	3	1	0.38	0.28	1	0.21	0.31	0	0.35	0.28	0	0.22	0.31	0	0.34	0.22	0	0.32	0.27	1	0.39	0.27	1	
9	B/OVijaya klakshmi	2950	normal	male		11	Term	1	0	0.44	0.51	0	0.53	0.4	0	0.59	0.41	0	0.47	0.58	0	0.52	0.41	0	0.59	0.43	0	0.51	0.41		0
10	B/O Neelavathy	1900	normal	female	4	13	PRETERM	3	1	0.24	0.35	0	0.23	0.39	0	0.24	0.36	0	0.29	0.37	0	0.29	0.39	0	0.34	0.39	1	0.27	0.36	1	
11	B/O durga	2240	normal	male	4	9	PRETERM	3	1	0.25	0.34	1	0.39	0.33	0	0.36	0.24	0	0.27	0.39	0	0.39	0.29	0	0.39	0.34	1	0.36	0.27	1	
12	B/O PRIYA	2650	normal	male	4	7	TERM	3	1	0.26	0.36	0	0.28	0.33	0	0.24	0.29	0	0.29	0.39	0	0.27	0.31	0	0.24	0.38		0.24	0.35	1	
13	B/O ASHA	2870	normal	female	4	11	TERM	3	1	0.36	0.27	0	0.31	0.29	0	0.34	0.24	0	0.39	0.27	0	0.31	0.25	0	0.35	0.23	1	0.35	0.24	1	
14	BAVINRAJ	2570	normal	male	7	14	TERM	1	0	0.45	0.56	0	0.47	0.51	0	0.41	0.59	0	0.47	0.58	0	0.42	0.52	0	0.49	0.58	0	0.56	0.54		0
15	B/O Prathiksha	2960	lscs	female	7	5	Term	1	1	0.57	0.44	0	0.52	0.44	1	0.58	0.48	0	0.57	0.42	0	0.51	0.47	0	0.52	0.47	1	0.55	0.43		0
16	B/o sathya	2850	lscs	male	5	12	Term	2	0	0.44	0.38	0	0.45	0.37	0	0.42	0.35	0	0.41	0.39	0	0.45	0.31	0	0.48	0.36	0	0.45	0.34	1	
17	B/O Rajeev	2550	normal	male	7	14	Term	1	1	0.28	0.38	1	0.24	0.36	1	0.21	0.39	1	0.28	0.36	1	0.27	0.34	1	0.26	0.36	0	0.57	0.56		0
18	B/O Ayisha	2140	normal	male	7	11	Preterm	1	0	0.35	0.26	0	0.31	0.28	0	0.36	0.27	0	0.31	0.29	0	0.37	0.28	0	0.26	0.37	0	0.47	0.49		0
19	B/O kala	2770	lscs	male	7	14	Term	1	1	0.26	0.38	1	0.27	0.32	1	0.27	0.34	0	0.29	0.35	0	0.28	0.39	0	0.25	0.33	0	0.44	0.49		0
20	B/O sangeetha	3100	normal	female	5	8	Term	2	1	0.41	0.34	1	0.45	0.31	1	0.48	0.34	1	0.44	0.38	1	0.41	0.37	1	0.46	0.31	1	0.42	0.36	1	
21	B/o krishanaveni	1750	normal	male	6	10	Preterm	2	0	0.35	0.49	0	0.31	0.48	0	0.34	0.48	0	0.38	0.44	0	0.37	0.41	0	0.31	0.46	0	0.32	0.49	1	
22	Neyamattula	2900	normal	male	4	10	term	3	1	0.23	0.33	1	0.27	0.36	0	0.27	0.39	0	0.21	0.33	0	0.27	0.34		0.25	0.36		0.25	0.34	1	
23	b/o Ashmitha	1900	normal	male	6	8	Preterm	2	0	0.34	0.44	0	0.42	0.33	0	0.34	0.48	0	0.47	0.39	0	0.39	0.44	0	0.31	0.46	0	0.35	0.47	1	
24	B/O Maala	2580	lscs	male	5	12	term	2	1	0.44	0.35	1	0.43	0.39	1	0.41	0.38	1	0.48	0.38	1	0.43	0.41	1	0.48	0.36	1	0.45	0.36	1	
25	B/o Alamelu	2650	normal	female	5	10	Term	2	1	0.38	0.47	1	0.31	0.48	1	0.36	0.47	0	0.38	0.47	0	0.37	0.47	0	0.37	0.49	0	0.36	0.45	1	
26	b/o mala	2110	normal	male	7	9	Preterm	1	0	0.48	0.52	0	0.44	0.56	0	0.41	0.57	0	0.42	0.52	0	0.49	0.53	0	0.41	0.59	0	0.47	0.57		0
27	b/o radhika	2000	normal	male	4	10	Term	3	1	0.22	0.32	1	0.25	0.36	0	0.24	0.37	0	0.23	0.38	0	0.22	0.39		0.21	0.34	1	0.23	0.34	1	
28	b/o kala	2520	normal	male	6	8	Term	1	1	0.42	0.54	1	0.44	0.52	1	0.51	0.59	1	0.47	0.51	1	0.44	0.53	1	0.4	0.55	1	0.53	0.55		0
29	B/O dillirani	2140	normal	male	5	10	preterm	2	0	0.43	0.33	0	0.34	0.41	0	0.48	0.32	0	0.47	0.35	0	0.49	0.31	0	0.48	0.58	0	0.51	0.59	1	
30	B/o poorna	1990	normal	male	6	11	Preterm	2	0	0.33	0.43	0	0.41	0.34	0	0.42	0.38	0	0.35	0.47	0	0.31	0.49	0	0.58	0.48	0	0.59	0.51	1	
31	b/o rani	2780	lscs	female	7	8	Term	1	0	0.41	0.57	0	0.56	0.41	0	0.59	0.4	0	0.48	0.513	0	0.57	0.43	0	0.59	0.43	0	0.52	0.55		0
32	b/o pushpa	1890	normal	male	6	9	Preterm	2	1	0.37	0.49	1	0.46	0.47	1	0.31	0.49	1	0.33	0.48	1	0.39	0.49	1	0.37	0.41	1	0.38	0.49	1	
33	B/o muthama	2510	normal	female	7	6	Term	1	0	0.51	0.42	0	0.49	0.53	0	0.55	0.47	0	0.46	0.51	0	0.59	0.4	0	0.57	0.48	0	0.51	0.43		0
34	B/O sangeetha	2050	normal	male	5	7	preterm	2	0	0.42	0.34	0	0.39	0.47	0	0.48	0.39	0	0.34	0.48	0	0.37	0.47	0	0.35	0.48	0	0.39	0.5	1	
35	B/o maala	2140	normal	male	7	8	Preterm	1	0	0.47	0.58	0	0.51	0.45	0	0.47	0.58	0	0.47	0.52	0	0.51	0.43	0	0.45	0.56	0	0.48	0.57		0
36	b/o Krishna	2950	normal	male	7	10	Term	1	0	0.58	0.47	0	0.45	0.51	0	0.58	0.47	0	0.47	0.52	0	0.53	0.41	0	0.56	0.44	0	0.54	0.56		0
37	B/o najma	2700	normal	female	5	11	Preterm	2	0	0.34	0.46	0	0.32	0.47	0	0.39	0.49	0	0.31	0.42	0	0.35	0.49	0	0.39	0.5	0	0.31	0.5	1	
38	B/O nazeeera	2800	normal	male	7	12	TERM	1	1	0.5	0.4	0	0.58	0.44	1	0.52	0.43	0	0.58	0.47	0	0.5	0.41	0	0.52	0.48	0	0.51	0.52		0
39	B/O JA0NI	2750	lscs	male	6	10	TERM	2	0	0.48	0.34	0	0.32	0.42	0	0.48	0.35	0	0.37	0.43	0	0.49	0.3	0	0.41	0.36	0	0.47	0.36	1	
40	B/O ramya	2910	normal	male	7	8	TERM	1	1	0.49	0.56	1	0.42	0.58	0	0.41	0.56	0	0.48	0.56	0	0.47	0.51	0	0.47	0.59	0	0.48	0.55		0
41	B/O sathya	2280	normal	female	6	9	Preterm	2	0	0.45	0.32	0	0.36	0.48	0	0.49	0.34	0	0.48	0.31	0	0.49	0.32	0	0.45	0.38	0	0.48	0.36	1	
42	b/o priya	2580	normal	male	6	11	Term	2	0	0.32	0.45	0	0.38	0.46	0	0.34	0.5	0	0.32	0.41	0	0.36	0.48	0	0.36	0.55	0	0.33	0.46	1	
43	b/o rama	2650	normal	male	4	12	Term	3	1	0.3	0.25	0	0.36	0.24	1	0.39	0.26	0	0.4	0.33	1	0.33	0.21	0	0.32	0.26	1	0.31	0.24	1	
44	b/o sathi	2960	normal	female	5	11	Term	2	1	0.36	0.48	0	0.42	0.38	1	0.34	0.42	0	0.35	0.48	1	0.24	0.41	0	0.36	0.45	1	0.55	0.38	1	
45	b/o devi	2110	normal	male	7	12	Preterm	1	0	0.56	0.41	0	0.42	0.52	0	0.53	0.45	0	0.43	0.51	0	0.59	0.42	0	0.53	0.42	0	0.56	0.56		0
46	b/o karthi	2930	lscs	female	7	11	Term	1	0	0.41	0.56	0	0.42	0.52	0	0.55	0.43	0	0.41	0.52	0	0.52	0.42	0	0.42	0.58	0	0.52	0.55		0
47	b/o anitha	1960	normal	female	7	7	Preterm	1	1	0.45	0.52	0	0.54	0.43	1	0.42	0.54	0	0.51	0.4	0	0.52	0.48	0	0.48	0.55	1	0.52	0.41		0
48	b/o priya	3010	normal	male	5	11	Term	2	1	0.41	0.32	1	0.45	0.363	0	0.46	0.36	1	0.47	0.38	0	0.47	0.32	1	0.32	0.46	1	0.42	0.33	1	
49	b/o aishwarya	2960	normal	female	4	8	Term	3	1	0.32	0.21	1	0.33	0.22	0	0.25	0.36	1	0.37	0.24	0	0.24	0.37	1	0.36	0.29	0	0.33	0.22	1	
50	b/o ramya	3000	normal	male	6	9	term	1	0	0.45	0.55	0	0.55	0.42	0	0.49	0.44	0	0.5	0.53	0	0.48	0.4	0	0.48	0.41	0	0.43	0.44		0
							0- NO ABNORMALITY																								

URKUND

Urkund Analysis Result

Analysed Document: usha thesis DTI & HIE.docx (D42768930)
Submitted: 10/19/2018 11:31:00 AM
Submitted By: usha.miracle2012@gmail.com
Significance: 7 %

Sources included in the report:

Dr.Rahul Gupta MD PEDIATRICS .docx (D42624011)
Dr.Rahul Gupta MD PEDIATRICS .docx (D42680538)
Doc1.docx (D41930645)
intro to conclusion.pdf (D42276681)
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2766891/
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4933547/

Instances where selected sources appear:

17

INSTITUTIONAL ETHICS COMMITTEE
GOVT. KILPAUK MEDICAL COLLEGE,
CHENNAI-10
Protocol ID. No. 14/2017 Meeting held on 08.06.2017

The Institutional Ethical Committee of Govt. Kilpauk Medical College, Chennai reviewed and discussed the application for approval "**Prospective Study of Diffusion tensor Imaging and Conventional Magnetic Resonance Imaging in Term and Preterm Neonates with Hypoxic Is chemic Encephalophy and Correlation with Clinical Outcome"** submitted by Dr.S.Usha, Post Graduate, Department of Radiodiagnosis, Govt. Kilpauk Medical College and Hospital, Chennai-10.

The Proposal is **APPROVED.**

The Institutional Ethical Committee expects to be informed about the progress of the study any Adverse Drug Reaction Occurring in the Course of the study any change in the protocol and patient information /informed consent and asks to be provided a copy of the final report.

30.6.2017

DEAN
Govt. Kilpauk Medical College,
Chennai-10.

23/6/17

ME 1 Sec> Ethical Committee